THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—25TH YEAR. SYDNEY, SATURDAY, FEBRUARY 12, 1938. No. 7.

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THE TREATMENT OF CERTAIN TUMOURS OCCURRING IN THE REGION OF THE OPTIC CHIASM.

By HUGH C. TRUMBLE, M.C., M.B., B.S., F.R.C.S., F.R.A.C.S.,

Surgeon to In-Patients, Alfred Hospital; Surgeon to the Austin Hospital; Consulting Surgeon to the Eye and Ear Hospital, Melbourne.

IT is perhaps not yet generally appreciated by members of the medical profession that nowadays the lot of a person afflicted with an intracranial tumour is not nearly so desperate as it was before the beginning of this century. Immense strides have been made in the matter of diagnosis, so that the presence of a tumour may be demonstrated in most cases at a reasonably early stage. Accurate localization is possible as a rule, and the nature of the growth may be predicted frequently with a degree of confidence hitherto unjustified. Because of the improvement in diagnosis and localization, the surgeon is now able to attack the tumour directly in the great majority of cases, and, indeed, there are few parts of the brain from which tumours have not been removed successfully. Surgical technique has improved to such an extent that in skilled hands operations which but a few years ago were so desperate as to be almost unjustifiable, are commonly brought to a successful conclusion in a most heartening way. The frame of mind engendered in physicians of bygone days by an almost unbroken series of dismal surgical failures—a frame of mind which found expression in some such remark as: "Oh, let the poor devil die a natural death!"—is no longer justifiable. Sir Victor Horsley once exhibited certain patients upon whom he had operated for the relief of intracranial tumour. A physician, who

in view of the difficulties with which the surgeon had had to contend was more witty than sympathetic, remarked that these were not "cures" but "survivors". It is true that a successful removal of a tumour may not restore the patient to perfect health, but this is not always so. It behoves practitioners to see that the diagnosis is made early, so that a favourable opportunity for really satisfactory surgical intervention may not be missed.

The question of "operability" of intracranial tumours has been discussed in numerous papers by neurologists and neurosurgeons of vast experience. A fair summary and extensive bibliography will be found in Bailey's book, "Intracranial Tumours".[1] In this country, Cox[2] has analysed a series of cases from various points of view. Before adopting the melancholy outlook of the physicians of a former day, the present-day practitioner should at least delve in the literature. It is an arresting fact that the percentage mortality in a large series of patients with acoustic tumour operated upon by Harvey Cushing is less than that in acute appendicitis at the present time. The treatment of adenomata of the pituitary gland is almost equally satisfactory.

On the other hand, there are many tumours which are highly malignant, so that attempts at removal are ultimately of little avail. Others, possibly of a relatively benign type, may be so situated that any direct attack upon them is inadvisable because of the grave dangers to life involved or because manipulations would so damage important structures as to cripple the patient, making him, indeed, merely a "survivor". If the surgeon unwisely attempts too much he will succeed only in bringing discredit upon a branch of surgery much in need of encouragement. It may be well to emphasize the point that there are tumours and tumours, and that to expect the surgeon to cope successfully with malignant growths in the brain when he is usually unable to deal with cancers in much more accessible and less important organs, is unreasonable.

The organization and equipment of an ordinary operating theatre are quite inadequate for the proper conduct of an operation upon the brain. Further, the surgeon and his team of assistants, nurses and porters, must be highly trained, as success depends upon the efficiency of all and upon close attention to detail. Brilliant operating finds no place here, its place being taken by thoughtful preparation, patience, gentleness and care in all manœuvres. Hæmostasis is all important, and no bleeding, however trivial, must be permitted to continue an instant longer than can be avoided. The surgeon advances tiny step by tiny step, regardless of time, sparing no pains to prevent loss of blood and the development of a condition of shock. Naturally, operations are often prolonged. Neurosurgeons have been accused of pottering. If any reply is necessary, it is to be found in the fact that patients are commonly returned to the ward in good condition after many hours upon the operating table, during which time the proper surgical procedure has been brought to a successful conclusion. How often has it happened that, with a speedy operator in charge, the patient has been returned to bed at the end of an hour or two in a state of collapse, so that he must fight for a chance to appear again, this time with added risks, as the protagonist in a terrible drama,—or tragedy! The skilled surgeon does not potter. He has much to do and does it gently and quickly. The speedy, unskilled surgeon is apparently quicker because he neglects to attend to innumerable small details which escape his notice.

In view of the fact that in Australia the surgery of the brain has not been developed to such a degree as in certain other countries, it may not be amiss to publish the case notes of a number of patients subjected to operation for the relief of intracranial tumour. Because of the smallness of the series, no conclusions as to the relative frequency of occurrence of different types of tumour or percentage mortality following operation are of any value. It seems better merely to record case notes in brief and to let the reader draw his own conclusions. If he is interested, he may read papers by surgeons of much greater experience. In this paper certain tumours growing in the region of the optic chiasm alone are dealt with.

Tumours Occurring in the Region of the Optic Chiasm.

In the region of the optic chiasm adenomata of the pituitary gland occur much more commonly than other tumours. Cysts and tumours arising in remnants of Rathke's pouch are next in order of frequency of occurrence, whilst much more rarely are found meningiomata, arachnoidal cysts, cholesteatomata, gliomata of the chiasm *et cetera*.

In addition, there occur tumours of uncertain nature and origin, which are grouped together for the purpose of this paper as unclassified tumours. Dr. Willis discusses the pathology of the tumours occurring in this series in a paper appearing in this issue of the journal.

Symptoms and Signs.

Certain symptoms and signs may be caused by interference with the normal functioning of the pituitary gland. Hypopituitarism commonly results from pressure of a tumour or cyst upon the hypophysis. The resulting clinical picture is greatly influenced by the age of the patient, and is well known. Hyperpituitarism is found in association with certain adenomata which contain a high proportion of eosinophile cells. Acromegaly results.

Pressure of tumours upon important structures, such as the optic chiasm, tracts and nerves, and nerve centres in the infundibulum and hypothalamus, is responsible for other effects, notably loss of vision, hypersomnia, changed mentality, and so on.[3] No attempt will be made in this paper to indicate the actual site of the damage which is responsible for any particular symptom. Suffice it to say that it is not wise to dogmatize at the present time, and that sometimes one cannot say whether a certain abnormality is due to under-

action or over-action of the pituitary gland, or to disturbance of the complicated nervous mechanism in the hypothalamic area of the brain.

Indications for Operation.

Most tumours growing in the region of the optic chiasm sooner or later cause loss of vision by pressing upon the optic nerves, chiasm or tracts. When this occurs, operation should be undertaken forthwith in order to relieve the pressure and to prevent further loss of vision, excepting when it is thought that the tumour is growing actually in the nerve substance. Operation is then useless. In other cases (for example, Case XX) pressure upon the hypothalamus may cause the most prominent symptoms and operation is again necessary. Surgical interference is occasionally called for in the treatment of acromegaly, even when there are no signs of pressure upon neighbouring structures. Constitutional changes of great severity may menace the life of the patient, and if radiotherapy fails to control them, operation is imperative and should not be delayed too long. Early operation in Case XII might have saved the patient's life.

As a rule, pituitary adenomata, neither causing pressure on neighbouring structures nor increasing degeneration of vital organs, such as the heart, do not call for surgical interference. Radiotherapy is frequently beneficial, but its unskilful application may be worse than useless. It should seldom or never be advised when there are signs of pressure upon the visual tracts. Cysts of Rathke's pouch, meningiomata and arachnoidal cysts necessitate operation whenever pressure signs arise. No other treatment is of the least avail.

Surgical Management.

In all cases of this series the approach has been by way of the right frontal region. The trans-sphenoidal route has been largely abandoned because in expert hands the risks entailed by the trans-frontal operation are no greater, and it is possible to see the disposition of the tumour and to remove that part of it which is actually pressing upon the optic nerves. Sometimes, as in Case XX, the tumour may be thought to be a pituitary adenoma, whilst it is in fact a "craniopharyngioma". Mere opening of such a cyst from the nose would afford but very temporary relief, it being necessary to remove as much of the wall as possible. A clear view of the region is essential. There are also other tumours which grow in the region of the optic chiasm, such as meningiomata of the *tuberculum sellæ*, the removal of which is not possible by the trans-sphenoidal route. The scar left after operation by the trans-frontal route is almost entirely above the hair line and almost unnoticeable (Figure I).

The right side is chosen for operation in right-handed persons, the left in left-handed, in order to avoid damage to the more important hemisphere. Should the frontal sinuses be very large, as they are sometimes in acromegalic persons, the approach is from the fronto-temporal region.

Actual details of technique vary with the surgeon, and will not be discussed here. Removal of the tumour substance is usually carried out by curettage and suction after incision of the capsule in front of the chiasm. As much of the capsule as possible is then removed. This is essential when dealing with cystic "craniopharyngiomata", in order to prevent the cyst from forming again. The cyst or tumour may bulge into the third ventricle and press upon the hypothalamus. When this is the case, removal is occasionally followed by unpleasant and dangerous complications, such as hyperthermia, which may be fatal. It is to be remembered that too radical a removal of an intrasellar tumour may leave the patient without sufficient pituitary gland substance. The chief object of the surgeon is to relieve pressure on the optic nerves and chiasm. Tumour substance is always left behind, which will grow again and which may necessitate further operative interference at a later date.

FIGURE I.
Photograph of patient, Case II, to show the insignificance of the scar left after operation.

Results of Operation.

As a rule, operations for the partial removal of adenomata of the pituitary gland are well tolerated, and it is not unusual for the patient to be allowed up in seven days. Of the twenty patients comprising this series, three died before leaving hospital. One patient (Case XVII) had been operated upon elsewhere three years previously, when a small amount of tumour tissue had been removed. At *post mortem* examination he was found to have an enormous tumour mass eroding the bones of the base of the skull and pressing deeply into the base of the brain (Figure VII). The great size and malignant nature of the tumour were not suspected, otherwise operation would not have been undertaken. A second patient died twelve days after an operation which had presented but little difficulty and which had been conducted quite satisfactorily (Case XVI). The third patient presented all the signs of an advanced acromegalic state, with gross enlargement of his heart. He had been in hospital for weeks

with severe heart failure (Case XII). Operation should have been undertaken a year or two earlier, when it might have been of immense benefit. In acromegaly, just as in toxic goitre, operation should be advised before vital organs are seriously damaged.

Recovery of vision is very striking as a rule. When the visual loss is of short duration, even though of severe degree, relief of pressure by skilful removal of a tumour is likely to be followed by substantial recovery (Case II). If for any reason treatment is long deferred, fibres in the visual tract degenerate and no great improvement in vision follows a tardy operation (Cases III and X).

Adequate removal of tumour substance in acromegalic patients helps to check the onward march of the disease, and even results in a certain improvement, more particularly as regards the skin and subcutaneous tissues, which become less coarse in texture. Symptoms and signs due to pressure of a tumour upon the hypothalamus, such as drowsiness, changes in mentality and so on, may be completely relieved by a successful operation, if not too long delayed (Cases VI and XX).

Adenoma of the Pituitary Gland without Hyperpituitarism.

In the group comprising adenoma of the pituitary gland without hyperpituitarism there were nine patients. In two cases symptoms recurred and a second operation was undertaken, making eleven operations in all. Two of the other patients had been operated upon previously by the transsphenoidal route by other surgeons. All of the patients are still alive. Operation was undertaken in each case for the relief of pressure exerted by the tumour upon neighbouring structures, usually the optic nerve fibres. The results have been very satisfactory, excepting in the case of those patients with very large growths. When the tumour has spread widely beyond the confines of the pituitary fossa, the difficulties of surgical removal are very great, if not insurmountable, and the results are not so good as they are when the tumour is of smaller dimensions. In Cases I, III and IV of this group the tumours were very large, in each instance the patient being blind in one or both eyes. At operation in Case III a large amount of soft glandular tissue was removed without much trouble, but in the other two removal was difficult because of the tough fibrous nature of the growths in which the optic nerves were embedded. Curettage and suction failed to make much headway, so that it was necessary to cut the tissue away piecemeal with punches and scissors. Unfortunately, in Case IV, at the second operation the right optic nerve was damaged, and the patient, though relieved of headache, was left totally blind.

CASE II.—Case II was one of pituitary adenoma causing gross loss of vision and signs of hypopituitarism. Partial removal was effected, with complete recovery of vision.

J.N.Y., a man, thirty-two years of age, was referred in May, 1934, by Dr. Archie Anderson and Dr. L. B. Cox. He complained that his vision had been failing rapidly for three months. Eighteen months previously his eyesight had been tested and passed by a medical officer of the railways. He had vomited at times. He had had no headaches. For some years he had had no sexual desire. Sleep had been normal. For a period some months previously he had passed urine several times at night, but this nocturia had recently ceased.

On examination he was found to be quite normal mentally. His skin was pale, fine and soft; his hands were rather podgy. Hair distribution was normal. There was no abnormality of the nervous system excepting in the eyes. Examination on May 21, 1934, showed that the pupils were of equal size and reacted, the right rather slowly, to light and accommodation. The fundi were normal in appearance. Vision in the right eye was reduced to perception of hand movements in the nasal field. In the left eye it was $^6/_{12}$. Plotting of the left field with a one millimetre white object disclosed an almost complete temporal loss, although the field was practically normal when tested with a two millimetre test object (Figures II and III).

X ray examination showed the *sella turcica* to be enlarged in a way suggesting the presence of an intrasellar growth.

Operation was undertaken on June 1, 1934. A bulging cystic tumour was found from which clear fluid was aspirated. Curettage was then carried out, bleeding was controlled, and the wound was repaired. Convalescence was uneventful and the patient left hospital on June 18, 1934. On the same day vision had recovered completely, being on the right side $^6/_6$ and on the left $^6/_4$. Fields to a one millimetre white object were normal.

On April 6, 1936, vision was $^6/_4$ (partly) in both eyes. In July, 1937, he wrote to say that he was in splendid health and that his vision was excellent.

Certain points in this case are worthy of comment. The field defect on the left side could easily have been missed. It was suspected by Dr. Anderson when the patient made errors on examination before a Bjerrum screen at a distance of one metre. Casual examination of fields may result in serious error. Failure of vision was rapid and gross, so that the patient was soon forced to seek medical aid. Pressure being relieved by operation, recovery of vision was complete, because there had been no gross degeneration of fibres of the visual tracts. A very different state of affairs was unfortunately allowed to develop in the case of the next patient, to his great detriment.

CASE III.—Case III was one of pituitary adenoma of large dimensions, causing gross loss of vision, exposed at operation and removed in great part, with striking improvement.

L.A., a German Jew, aged forty-six years, was referred by Dr. Edward Ryan on May 9, 1935. Two years before this date his vision began to fail, first in the right eye, later in the left eye. His eyes were examined in London and his blood was tested on several occasions and found to be normal (Wassermann test). Early in the year 1935 his vision failed rapidly and soon he was almost totally blind. He had no headache at any time. He arrived in Melbourne in March, 1935. Dr. Ryan noted extensive degeneration of the retinæ and atrophy of the optic disks. X ray examination revealed ballooning of the *sella turcica*, suggesting the presence of a large intrasellar tumour. The patient was stoutish, with a fine, delicate skin and fresh complexion. His hair was normal in distribution, but fine in texture. Apart from the eyes, there was nothing abnormal detected by an examination of the nervous system. His pupils were semi-dilated and did not react to light stimulus. Optic atrophy was present on both sides, and there were scattered patches of chorioido-retinitis. Vision was limited to bare perception of light in the right eye and hand movements in the left eye. The Wassermann test gave no reaction.

Operation was undertaken on May 11, 1935, under ether anæsthesia given by the intratracheal method. The approach was by the usual right frontal route.

Convalescence was uneventful except for an acutely painful affection of the right acromio-clavicular joint which came on a week after operation. This soon subsided.

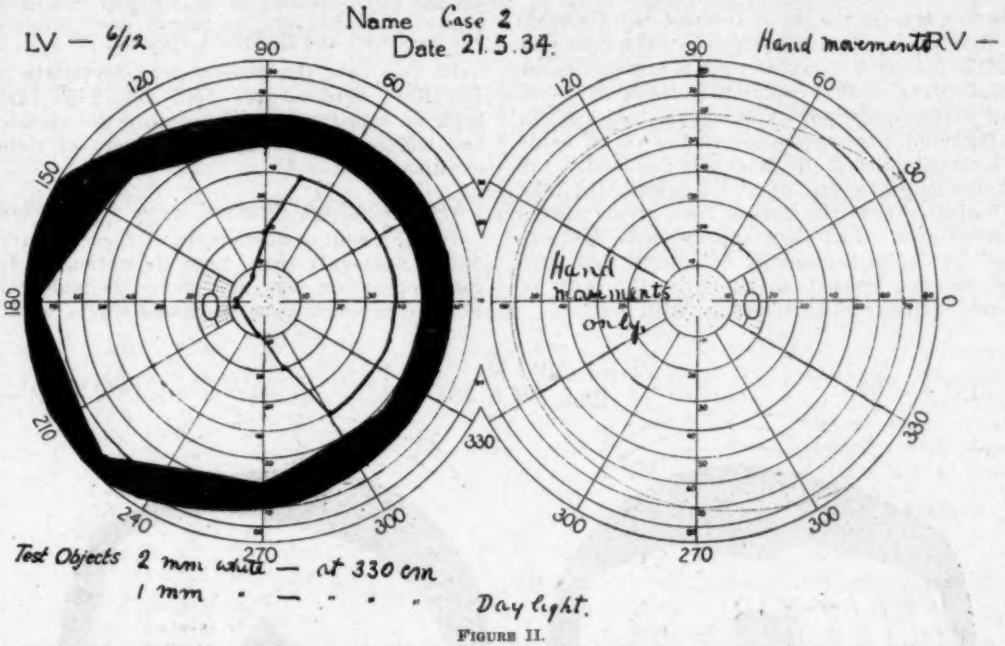

FIGURE II.

Fields of vision, Case II, before operation. In the left eye the field, which was normal when tested with a two-millimetre object, showed an almost complete temporal loss with a one-millimetre test object. The right eye was almost blind.

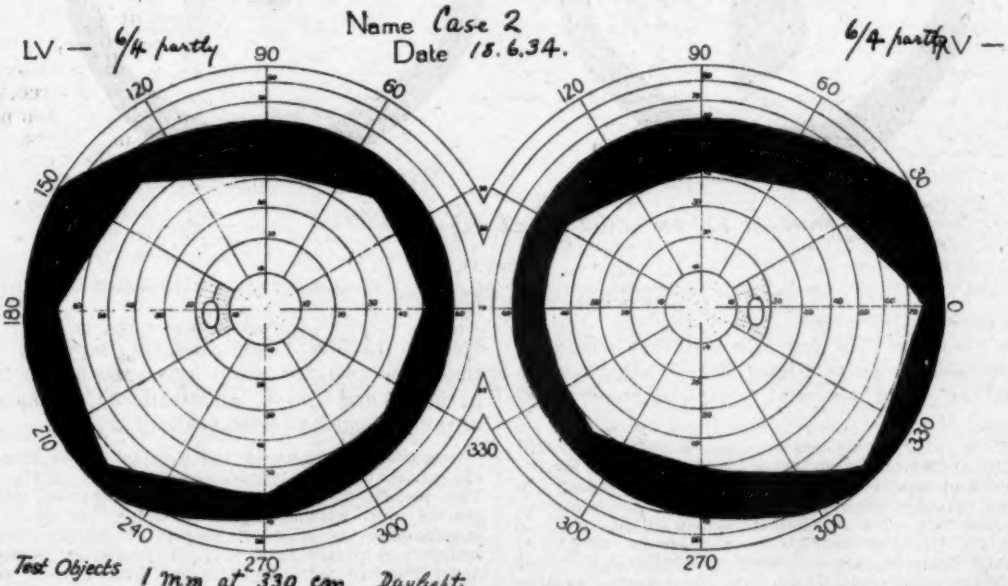

FIGURE III.

Fields of vision, Case II, after operation, showing complete recovery.

A very large tumour was found rising out of the pituitary fossa and compressing the optic nerves and chiasm. The capsule of the tumour was incised and a large amount of soft tumour substance was curetted and sucked away. The wound was repaired.

A month later vision was much improved so that the patient could get about unaided. He was, however, unable to read. In September, 1936, vision with correction was $^{6}/_{36}$ in the left eye. In July, 1937, the patient reported that he was very well and able to get about unaided. He could

read the headings in the newspapers and from the front row of the stalls could see well enough to enjoy a visit to the "movies".

There are several points of interest in this case. In the first place, a serious error in diagnosis was responsible for great delay and gross destruction of the visual tracts, so that complete recovery of vision was out of the question. A skiagram taken at an early stage and an examination of the visual fields would have established the diagnosis. Secondly, the remarkable improvement of vision which did take place, indicates that the nerves have great powers of recovery even when they appear to be severely damaged. Thirdly, the case is notable in that such a large tumour caused so little in the way of symptoms, apart from interference with vision.

Convalescence was uneventful, and the patient was allowed up on the ninth day after operation. On December 12, 1935, vision had improved to $^6/_4$ (partly) in the right eye and to $^6/_9$ (partly) in the left eye. The fields were normal. In June, 1937, the patient wrote to say that he was very well and his vision splendid.

In this case the patient was fortunate in that Dr. Kerr detected the field defect so early and referred him for operation before the visual nerves had suffered much. Hence recovery of vision was excellent.

Adenoma of the Pituitary Gland with Acromegaly.

In the group of adenomata of the pituitary gland with acromegaly there were six patients. In three cases operation was undertaken primarily for the relief of pressure upon the visual tracts, with failing vision. In one, vision was not improved, but in the other two the result was satisfactory. Three patients had grave constitutional changes with advancing cardiac degeneration.

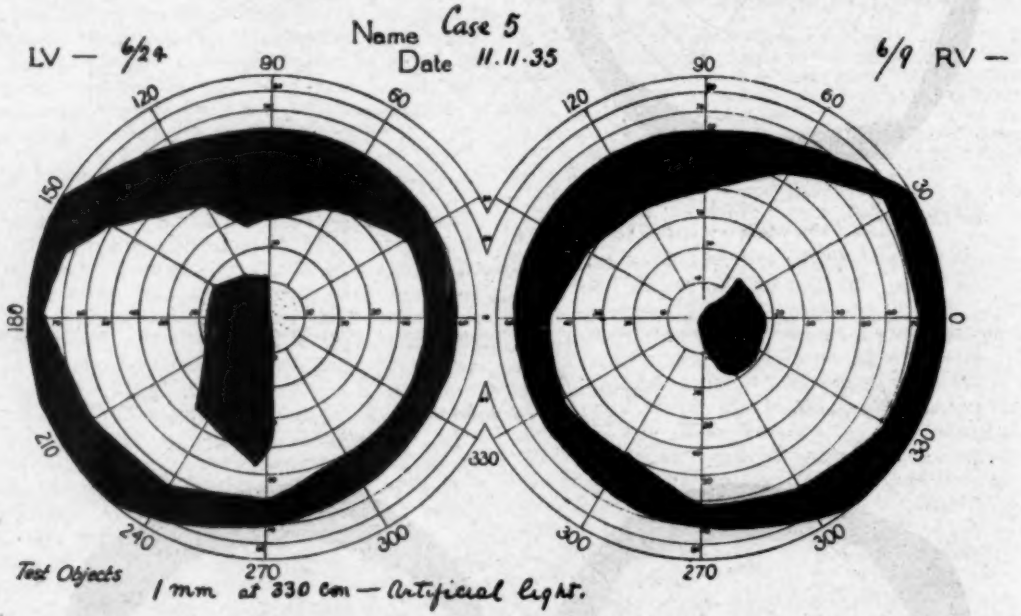

FIGURE IV.

Fields of vision, Case V, before operation. Scotomata suggesting a commencing bitemporal hemianopia. After operation there was complete recovery.

CASE V.—Case V is that of a pituitary adenoma, with excessive obesity and failing vision, partly removed at operation, with complete recovery of vision.

H.B.W., a man, forty years of age, was referred by Dr. L. B. Cox on November 10, 1935. He had always been a "fat boy" and now weighed more than twenty stone. He had been sexually impotent for some years. About two months previously his vision had become misty. He was seen by Dr. Kerr, of Bendigo, on October 14, 1935, who found that vision in each eye, with correction, was $^6/_6$, but that there were scotomata in each temporal field suggesting a commencing bitemporal hemianopia. With a one millimetre object the fields were normal to ordinary perimetry. On November 11, 1935, vision was reduced to $^6/_9$ in the right eye and $^6/_{24}$ in the left. The scotoma in the left temporal field had greatly increased in area (Figure IV).

Operation was undertaken on November 21, 1935. A cystic tumour was exposed, its liquid contents were aspirated, and soft broken down material was curetted and aspirated away.

Operation was delayed too long in one instance, until the patient became bedridden with acute cardiac failure. This patient died some hours after operation, which was carried out without much trouble. At *post mortem* examination the state of the field of operation was quite satisfactory, death being due to circulatory failure. The heart weighed thirty-eight ounces (the normal weight is about eleven ounces)[10] (Figures V and VI).

The other two patients are well, but sufficient time has not yet elapsed since operation to permit of any conclusions being drawn as to the degree and permanency of the beneficial results.

In most of the cases in this group operation was not undertaken until X ray treatment had been tried

TABLE I.

Brief Notes of Eight Cases of Pituitary Adenoma without Acromegaly.

Case Number.	Sex.	Age.	Chief Symptoms and Signs.	Operation.	Vision.		Remarks.
					Before Operation.	After Operation.	
I	M.	63	Blindness, gross mental degeneration. Epilepsy. Symptoms for more than 20 years.	(1) 14/2/31 (2) 11/4/36	Totally blind. Totally blind.	Blind. Blind.	Improved in mental capacity after second operation. Large fibrotic tumour.
II	M.	32	Rapid failure of vision for three months. Moderate hypopituitarism.	1/6/34	R. = Perception of hand movements. L. = 6/12.	6/4 partly. 6/4 partly.	Returned to work in railways. See Figures II and III. Full record in text.
III	M.	46	Failing vision for two years. Bilateral optic atrophy.	11/5/35	Perception of light barely.	L. = 3/60 10/9/36	Full record in text. In July, 1937, is well and able to get about unaided.
IV	F.	34	Failing vision for 18 months. Headache, mental changes.	(1) 23/8/35	R. = Record lost. L. = Blind.	Record lost. Blind.	Gross defect of right visual field before operation; much improved afterwards, but still showing upper temporal defect.
			Headaches recurred, right vision again failing.	(2) 20/4/37	R. = Record lost. L. = Blind.	Blind. Blind.	Second attempt to remove large fibrotic tumour resulted in damage to right optic nerve. Headache relieved. Mentality improved.
V	M.	40	Gross obesity since boyhood. Weighs more than 20 stone. Failing vision two months.	21/11/35	R. = 6/9. L. = 6/24.	6/4 partly. 6/6 partly.	Large central scotomata before operation: normal fields afterwards. Working as a butcher. Well in June, 1937. Figure IV.
VI	F.	38	Failing vision five years. Transsphenoidal operation elsewhere with improvement. Recurrence of symptoms with gross mental deterioration. Optic atrophy on left side.	30/1/36	R. = 6/18. L. = Perception of hand movements in nasal field.	6/5 partly. Less than 6/60.	Mentally normal after operation. Doing housework. (February, 1937.)
VII	M.	34	Failing vision for three years. Headache. Drowsiness. Moderate hypopituitarism.	21/4/36	R. = 6/12. L. = 6/60.	6/6. 6/6.	Right upper temporal scotoma before operation, much reduced afterwards. Working as a barber and very well in February, 1937. Vision 6/6 both eyes.
VIII	F.	47	Failing vision 10 years. Transsphenoidal operation elsewhere with improvement. Recurrence of symptoms.	22/4/37	R. = 6/5. L. = 6/12.	6/5. 6/12.	Right field showed gross temporal loss before operation and became almost normal afterwards. Left field contracted after operation. General health excellent.
IX	F.	53	Severe pain in region of left eye. Drowsiness and failing memory. Epileptic fits.	23/7/37.	R. = 6/9. L. = 6/9.	6/9. 6/9.	Much more alert soon after operation. No longer drowsy.

NOTE.—Cases I and VI of this group have been reported in detail in a paper by Dr. Cox.[1] Vision with correction is recorded in the table in all cases.

very thoroughly. It is interesting to note that even after prolonged treatment by X rays the pituitary gland may appear to be very active (see report on Case XII in Dr. Willis's paper).

CASE X.—Case X is one of pituitary adenoma, causing loss of vision and an advanced degree of acromegaly, partially removed at operation, with improvement.

G.C., a man, thirty-three years of age, referred by Dr. Duncan, was admitted to hospital on October 29, 1934. He complained of failing vision. About ten years previously his weight was about eight stone. It increased until he weighed more than seventeen stone. Four years prior to his admission to hospital it was noted that he could not plough a straight furrow because of failing vision, and two years later he could not read. About this time he had a fit and was unconscious for some time. Headaches followed and had been severe and constant for the previous three months. He perspired excessively. Sexual power was not affected. During the year prior to his admission to hospital he had been drowsy and liable to fall asleep at any time.

On examination he presented most of the clinical features of an advanced acromegalic state. His weight was seventeen stone two pounds. Examination of his eyes disclosed that in the left eye vision was limited to perception of light. In the right eye vision was $^{6}/_{9}$ and limited to the nasal field.

Operation was undertaken on November 12, 1934, under local anæsthesia. A tumour rising out of the pituitary fossa was exposed and removed in large part by curettage and suction. Convalescence was uneventful, the patient being allowed out of bed on the eighth day after operation.

On December 3, 1934, vision in the right eye was $^{6}/_{60}$ and a one millimetre object could be seen with the left eye in a small area in the nasal field. On October 16, 1935, there was slight expansion of the fields and weight had decreased to sixteen stone. The patient's skin was of a finer texture and his fingers were less thickened than previously. He has not reported for examination since.

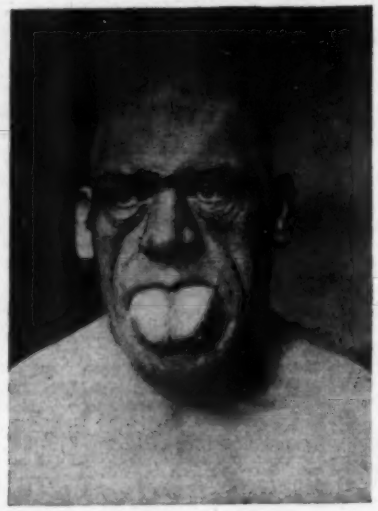

FIGURE V.
Photograph of a patient (Case XII) taken two years before the date of operation to show advanced state of acromegaly.

Extensive degeneration of the visual fibres had taken place before operation, so that much recovery of vision was not to be expected.

CASE XV.—Case XV was one of pituitary adenoma with advanced acromegaly, progressive cardiac degeneration and failing vision, subjected to operation, with improvement.

R.D., a woman, sixty-seven years of age, attended the Alfred Hospital for some years. She complained of blurring of vision and shortness of breath on exertion. In February, 1937, she presented signs of moderately advanced acromegaly. Vision in the right eye was $^{6}/_{60}$ in the left $^{6}/_{12}$. The visual fields were practically normal. The apex beat was in the fifth interspace four inches from the mid-line. There was a soft systolic murmur at the apex. The systolic blood pressure was 180 millimetres of mercury. Operation was advised, partly in order to prevent further cardiac deterioration and partly because of failing vision.

On May 27, 1937, the tumour was exposed, and a considerable amount of pinkish-white, soft, glandular material was removed. Recovery was uneventful.

On June 21, 1937, she stated that she felt very comfortable and that she was able to exert herself more without dyspnœa. Vision in both eyes was $^{6}/_{6}$ (partly).

Unclassified Tumours.

In the group of unclassified tumours there were three patients. Two died, one day and twelve days respectively, after operation.

One, a man, twenty-six years of age (Case XVII), had an enormous tumour of uncertain nature spreading widely over the base of the skull and brain (Figure VII).

The second patient (Case XVI), a woman, aged fifty-four years, was thought to have a pituitary adenoma causing loss of vision. Operation was carried out satisfactorily, but, after a stormy period of twelve days' duration, the patient died. The tumour is of doubtful nature, possibly a carcinoma secondary to a renal growth. The probability is heightened by the fact that during the second post-operative week there was severe hæmaturia.

TABLE II.
Brief Notes of Six Cases of Pituitary Adenoma with Acromegaly.

Case Number.	Sex.	Age.	Chief Symptoms and Signs.	Operation.	Vision.		Remarks.
					Before Operation.	After Operation.	
X	M.	33	Gross acromegaly with headache and failing vision. Bitemporal hemianopia. Symptoms for 10 years.	12/11/34	R. = 4/60. L. = Perception of light in nasal field.	4/60. Perception of light.	Right field of vision increased in area. Weight decreased from more than 17 to 16 stone (16/10/35).
XI	M.	27	Early acromegaly with failing vision and headache. Central scotomata both sides.	29/5/36.	R. = 6/5 partly. L. = 6/24.	6/6. 6/12 (18/3/37).	Headache relieved. Well in July, 1937. Driving truck.
XII	M.	42	Advanced acromegaly with extreme visceral degeneration and severe cardiac failure. Figure V.	4/6/36.	Normal.		Died one day after operation. Heart weighed 38 ounces. Figure VI.
XIII	M.	47	Advanced acromegaly with failing vision and hypersomnia. Optic atrophy on left side.	19/2/37	Record lost.	R. = 6/12. L. = Perception of hand movements.	General health improved. Vision improving slowly.
XIV	F.	35	Advanced acromegaly with visceral degeneration, not controlled by X rays.	17/5/37	R. = 6/9. L. = 6/9.		Operation primarily for relief of cardiac degeneration. Much improved.
XV	F.	67	Acromegaly with increasing visceral degeneration. Dyspnœa on exertion. Blurring of vision.	27/5/37	R. = 6/9. L. = 6/18.	6/6. 6/6.	Operation primarily for relief of cardiac degeneration. Much improved.

NOTE.—Case XII has been reported in detail by Dr. Cox[3] and Dr. Laurie.[4]

The third patient (Case XVIII) is well and vision has much improved. At operation a cystic tumour with a calcified wall was removed in part.

CASE XVI.—Case XVI was one of intrasellar tumour of doubtful nature, causing failing vision. Partial removal was effected. A stormy post-operative course was complicated by gross hæmaturia, failing blood pressure and death twelve days after operation.

W.G.B., a married women, fifty-four years of age, was referred on August 14, 1934, by Dr. Hudson. Her vision had been failing for eighteen months, and recently she had had frontal headaches of moderate severity. She had had no illness of any note and had ceased menstruating four years previously. She was a stout, strong looking woman with a rather coarse and highly vascular skin. Her hair was thick and rather coarse. Apart from her eyes, the nervous system seemed to be normal. The right pupil was slightly larger than the left, both reacting to light. Both disks showed changes of primary atrophy. Vision was $^6/_{36}$ in both eyes. Perimetry disclosed a complete bitemporal hemianopia.

Skiagraphic examination of the skull disclosed enlargement of the *sella turcica* with erosion of the *dorsum sellæ* and posterior clinoid processes, suggesting the presence of an intrasellar tumour.

A diagnosis of pituitary adenoma was made.

Operation was undertaken on August 23, 1934, under local anæsthesia. The right frontal sinus was opened accidentally. Bleeding was troublesome throughout the operation. A tumour was displayed bulging upwards from the *sella turcica* in front of the optic chiasm. A fair amount was curetted and sucked away. The patient was returned to bed in good condition.

During the next two days blood-stained cerebro-spinal fluid trickled into the mouth via the frontal sinus. The temperature rose to 104° F. on the second day, but fell to below normal on the third, after which it rose on the succeeding two days to 100° F. The blood pressure fell as the temperature rose, and remained at a low level from then on. Consciousness varied, the patient being at times restless, at others drowsy. She was disorientated and irrational most of the time, and passed urine into the bed. Lumbar puncture on several occasions showed the cerebro-spinal fluid to be tinged with blood, but no organisms were seen and culture produced no growth. As the days went by the temperature became subnormal, the pulse weak but not very rapid, and the blood pressure remained very low. After catheterization of the bladder on the sixth day the urine became brightly stained with blood, and remained so for several days. On the twelfth day after operation the patient died quietly, though she talked to the nurse a short time before her death and did not seem worse than she had been for some days.

The tumour is possibly an atypical adenoma of the pituitary gland, but may be a carcinoma secondary to a primary renal growth. In the absence of a *post mortem* examination, no primary growth could be demonstrated, but the profuse hæmaturia suggested a malignant tumour in the urinary tract. It is a disturbing fact that intracranial tumours frequently prove to be metastatic from an obscure primary carcinoma, which gives no clinical evidence of its presence. Secondary growths in the pituitary fossa are, however, very rare. After operation the patient passed into a state resembling that described as "hyperthermia", although her temperature did not rise about 104° F.

CASE XVII.—Case XVII is one of malignant tumour of the pituitary gland (probably), causing complete blindness, drowsiness and mental derangement. Death occurred after attempted removal. *Post mortem* examination revealed an enormous tumour mass spreading widely over the base of the skull.

R.H., a man, twenty-six years of age, was admitted to the Alfred Hospital on April 7, 1936. Three years previously he had been operated upon elsewhere for the relief of failing vision. A small amount of tumour substance was removed, which was thought to be part of a chromophobe adenoma of the hypophysis. The patient's sight was but little, if at all, improved after operation. Later he had fits, in which he became unconscious. Vision progressively failed. On admission to hospital he was able to shuffle about. He was pale, weak and rather childish in his bearing. He was unable to concentrate, was confused and unconcerned about the proposed operation. He was drowsy, and spoke in a childish, silly way, interrupting others in conversation and giggling inanely. He was quite blind, and the optic nerve heads were atrophied. The pupils did not react to light. The limbs were weak. There was no other abnormality of note disclosed by a neurological examination.

Radiographic examination showed that the *dorsum sellæ* had disappeared, and there appeared to be extensive erosion of bone in the region of the anterior clinoid processes.

Operation was undertaken on April 14, 1936. The tumour mass was exposed, but none of the usual landmarks, including the optic nerves, could be seen. Incision into the mass was followed by brisk hæmorrhage. This was controlled with some difficulty, and the operation was abandoned. The patient died on the following day. At *post mortem* examination an enormous tumour was disclosed which had eroded widely the bone of the base of the skull and grown laterally between the dura and skull beneath the temporal lobes (Figure VII). The tumour passed through the right superior orbital fissure into the right orbit, and bulged into the anterior fossa of the skull on the left side. It indented the base of the brain deeply, and reached caudally almost to the *foramen magnum*. The optic nerves were stretched round the mass and overlapped by it. The tumour was largely degenerated and of a semi-liquid consistency in great part. The nature of the tumour is uncertain.

This tumour was of much larger dimensions than had been suspected before operation. Anything approaching a total removal was out of the question, and it was unfortunate that operation was undertaken.

Tumours Arising in Remnants of Rathke's Pouch.

CASE XIX.—Case XIX was one of an adamantinoma exposed at operation and partially removed. Relief occurred for a short period. Death occurred two months after operation.

I.M., a girl, aged fourteen years, was admitted to hospital on July 13, 1933. In May, 1932, she had complained of headaches of a bursting nature, followed a little later by diplopia. In October she experienced attacks of vomiting, and her health became progressively worse. Two attempts were made by another surgeon to expose the supposed "craniopharyngioma" without success, except that the headache was relieved to some extent. Her weight increased considerably, she became very thirsty and hungry, and passed more urine than normal. She was an adipose little girl of poor mentality, with a monotonous fashion of speaking. Her breasts were not well developed, and her pelvis was narrow. Hair was not very abnormal in distribution or texture. Her hands were podgy, with tapering fingers. Vision was limited to perception of fingers at a distance of one metre. There appeared to be a left lower quadrantic field loss in both eyes. Optic atrophy was well marked in both eyes.

TABLE III.

Brief Notes of Three Cases of Unclassified Tumours in the Pituitary Region.

Case Number.	Sex.	Age.	Chief Symptoms and Signs.	Operation.	Remarks.
XVI	F.	54	Headaches, failing vision for 18 months. Optic atrophy. Bitemporal hemianopia. Vision with correction, 6/36 both eyes.	23/8/34: Satisfactory removal of tumour tissue from the pituitary region. Stormy post-operative course complicated by retention of urine and later profuse hæmaturia.	Died 12 days after operation. Tumour of doubtful nature. ? Secondary carcinoma.
XVII	M.	26	Totally blind. Optic atrophy. Gross mental degeneration.	14/4/36: Incision into tumour followed by brisk hæmorrhage. Operation abandoned.	Died on the day after operation. Enormous malignant tumour found at *post mortem* examination. Nature uncertain. (Figure VII.)
XVIII	F.	45	Failing vision for some years. Headache. Early primary optic atrophy. Deposits of calcium salts seen in skiagram above pituitary fossa. Loss of vision in right temporal field and in left upper temporal quadrant.	15/5/36: A cystic tumour with calcium deposits in its walls was evacuated and the wall removed in part, after curettage. Nature uncertain.	Vision improved. Before operation: R.V. = 6/9, L.V. = 6/24. With correction, 26/7/37: R.V. = 6/6, L.V. = 6/6. Right field of vision much enlarged, almost to normal. Some recovery in left temporal field.

Radiography showed that the *sella turcica* was enlarged and that there were opacities suggesting the presence of a partly calcified suprasellar tumour. A diagnosis of "craniopharyngioma" was made.

Operation was undertaken on July 14, 1933, under local anæsthesia. The bone flap made at the previous attempts was elevated, and a needle was passed into the right lateral ventricle. The patient's condition at this stage became poor, so that nothing more was done. On July 21, 1933, the wound was reopened and a cystic tumour was exposed. Its liquid contents were aspirated and a small part of its substance was removed. The patient's poor toleration of operative interference contraindicated any attempt at radical removal of the growth. After operation there was a decided improvement. The patient became more manageable and stated that her head felt comfortable. However, symptoms recurred in a few weeks, and she died on September 16, 1933. The brain was obtained, and is depicted in Figure VIII.

In this case the growth was not a simple cyst, but largely solid in structure. It had invaded and almost filled the third ventricle, and could scarcely have been removed, even had the patient been able to tolerate a difficult and prolonged operation. Aspiration of cysts of Rathke's pouch is seldom curative, although Cushing reports the case of a patient who remained well for many years thereafter. As much of the growth as possible should be removed.

CASE XX.—Case XX was one of "craniopharyngioma" causing loss of vision and hypersomnia. Removal of greater part of the tumour was effected, with relief.

A.B., a farmer, aged twenty-seven years, was referred by Dr. Loosli on June 6, 1935. Three years previously he had become listless and sleepy. Headache, usually frontal or vertical, followed and continued up to the present. His eyesight began to fail, mainly in the left eye. During the last six months he had vomited a few times and become very sleepy. Previously a jolly, cheerful person, he had ceased to take much interest in things. He could not be trusted to do anything on the farm, as he would go off and forget all about his duties. On one occasion when playing football he held up the game by standing stupidly on the field and neither taking part in the game nor moving out of the way of the others. He was a tall, well-developed young man, casual and rather flippant when not drowsy or asleep. His own account of his troubles was not reliable. His skin was rather pale and fine in texture. His hair grew strongly on his head, was scanty in the axilla and on the body, and had a female distribution on the pubic area. The external genitalia were small. He shaved only twice a week.

Mentally he was quite abnormal. He fell asleep at any time, and when roused his statements were unreliable and delivered in a flippant manner. He showed little respect for anyone and was at times quite unreasonable, so that an attempt to collect a specimen of blood had to be abandoned.

Examination of the nervous system disclosed a rotary nystagmus present on lateral and upward gaze. The left optic nerve head was atrophic, and although it was impossible to plot the fields accurately on account of the patient's mental state, it was obvious that he had a bitemporal hemianopia, absolute on the left side, partial on the right side.

A radiograph of the skull showed that the pituitary fossa was a good deal enlarged, with a depressed, thickened floor. The posterior clinoid processes were displaced posteriorly. There was no abnormal shadow in the suprasellar region.

It seemed clear that there was a tumour in the pituitary fossa growing upwards and pressing upon the optic chiasm and the hypothalamic region of the brain. It was likely to be pituitary adenoma of the chromophobe variety.

Operation was undertaken on June 13, 1935, under ether anæsthesia produced by the intratracheal method. A large cystic swelling was found rising from the pituitary fossa and thrusting the optic chiasm far backwards and upwards so that the optic nerves were much elongated. Five cubic centimetres of yellowish fluid were aspirated. The cyst was then opened, and its wall was stripped carefully from the chiasm and brain until it was attached only in the pituitary fossa. The slack wall was then excised, and the fossa, where probably part of the tumour had not been removed, was swabbed carefully with formalin (5%). The wound was closed carefully. The operation was completed in two and a half hours, and the patient was returned to bed in excellent condition.

Wound healing was rapid and untroubled, the last sutures being removed on the third day after operation. The temperature rose to 103·5° F. soon after operation, then gradually subsided in the course of the next five days. The systolic blood pressure rose from 90 to 110 millimetres of mercury and the pulse rate fell from 150 to 90 during the same period. The patient was very restless for the most part and did not sleep at all for three days, though given large doses of morphine, barbitone and "Luminal". He was quite unreasonable at times, and had to be restrained from getting out of bed. In his more normal periods he was amiable and quite unlike his former unpleasant self. He imagined at times that people were intent on harming him or members of his family. Gradually he improved mentally, and a month after operation he returned to Tasmania. He was seen again on November 16, 1935. He was practically normal mentally and able to undertake light duties on the farm. He wrote on July 19,

1937, to say that he was very well. Vision was good, being better in the right than in the left eye. He was able to work satisfactorily on a farm.

In this case the growth was removed almost completely. The change in the mental state of the patient was very extraordinary. The question of the effect of tumours at the base of the brain upon sleep and consciousness has been discussed at length by Dr. Cox.(2)

Acknowledgements.

Many of the patients in this series were referred for operation by Dr. L. B. Cox from the Neurological Clinic of the Alfred Hospital. Dr. R. A. Willis has taken a great deal of trouble in carrying out the pathological investigations. To both colleagues I am much indebted. It is a pleasure also to acknowledge the help given by Dr. Mushin and other members of the "neuro-surgical team".

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A PATHOLOGICAL STUDY OF TUMOURS OF THE PITUITARY REGION.

By RUPERT A. WILLIS, M.D., D.Sc. (Melbourne), M.R.C.P. (London).

(From the Baker Institute of Medical Research, and the Department of Pathology of the University, Melbourne.)

DURING the past five years, 23 tumours arising in the pituitary gland or in its immediate neighbourhood have been examined in the pathological department of the Alfred Hospital. Of the 23 cases, 20 were treated by operation, and in the following account these 20 cases are designated by the same numbers as in the companion paper by Mr. H. C. Trumble. Three of the surgically treated patients subsequently died and were examined *post mortem*; and in three additional cases, in which operation had not been performed, *post mortem* examinations were carried out. For microscopic study, paraffin sections were stained by hæmatoxylin and eosin and by Heidenhain's iron-hæmatoxylin and van Gieson's stain.

The following list shows the types of the 23 tumours studied.

Anterior lobe adenomata—		
(*a*) without acromegaly	9 cases	Total 16 cases
(*b*) with acromegaly	7 cases	
Tumours of doubtful nature		Total 4 cases
Tumours derived from remains of Rathke's pouch—		
(*a*) "Adamantinoma"	1 case	Total 2 cases
(*b*) Squamous epithelial cyst ..	1 case	
Fibrosarcoma of pituitary region		1 case

Each of these groups will be considered in turn, special attention being paid to difficulties encountered in histological diagnosis and to the tumours of doubtful nature.

Anterior Lobe Adenomata.

Of the 23 tumours, 16 consisted of epithelial glandular tissue derived from the anterior lobe of the gland. Although these are classed here as "adenomata", it seems probable that in many cases the growths are not true neoplasms, but rather examples of focal hyperplasia comparable with the nodular goitres of the thyreoid gland. Structural features suggesting this, features seen also in goitrous thyreoids, are: (*a*) non-encapsulation of the adenomatoid tissue in some at least of the cases, this tissue and the remaining normal part of the gland showing a gradual transition (see particularly *post mortem* Case 5302 and Figure II); (*b*) the frequent presence of regressive changes in the adenomatoid tissue, including atrophy of the epithelium, fibrosis, calcification and cyst formation, as in Cases I, V, VIII, XI, and *post mortem* Case 5302.

Adenomata from Non-Acromegalic Patients.

Clinical details of the nine tumours in the group of adenomata from non-acromegalic patients are given in Mr. Trumble's paper and are not referred to here. In all of the cases the tissues examined were obtained solely by operation. The histological diagnosis of several of these growths gave difficulty, and it was only when the entire series was reviewed later that a proper appreciation of the wide range of structure to be found in pituitary adenomata was attained.

CASE I.—A male patient, aged sixty-three years (reported by Dr. L. B. Cox, 1937, Case VI), had fragments of tissue removed in 1932; they had a microscopic structure compatible with chromophobe adenoma. The tissue removed in 1936 also showed chromophobe adenoma, with advanced degenerative changes, namely, hyaline fibrosis, areas of old and recent blood pigment and patchy calcification. The epithelial tissue was scanty and atrophic, and the fibrous stroma formed stout strands of dense hyaline tissue.

CASE II.—A male, aged thirty-two years, had a cellular vascular adenoma composed of faintly eosinophile cells.

CASE III.—A male, aged forty-six years, had a vascular chromophobe adenoma.

CASE IV.—A female patient, aged thirty-four years, had an adenoma of retiform structure somewhat resembling that of Case VII, that is, a network of narrow strands of spheroidal and elongated non-eosinophile epithelial cells, with intervening vascular and hyaline connective tissue strands.

CASE V.—From a male patient, aged forty years, fragments of tissue were removed from the wall of the cystic growth which showed chromophobe adenoma.

CASE VI.—A female patient, aged sixty-five years (reported by Dr. L. B. Cox, 1937, Case V), had some pieces of tissue removed in 1931; these had the structure of chromophobe adenoma with an architecture like that of the normal gland. Tissue removed in 1936 had a similar structure, though the epithelial cells now appeared to be faintly eosinophilic. The tissue was still healthy in appearance, with little or no degenerative change.

CASE VII.—A male patient, aged thirty-four years, had a growth which was an adenoma with ill-defined spheroidal and elongated cells arranged in narrow strands forming a fine network (Figure I). The cells were faintly eosinophile in parts. The stroma was partly vascular, partly hyaline, fibrous tissue.

CASE VIII.—From a patient aged forty-seven years scanty fragments from the wall of a large cystic growth included pieces of non-eosinophile adenoma with the epithelial cells arranged in prominent perivascular mantles.

CASE IX.—From a female, aged fifty-three years, fragments were removed which showed the structure of a well-preserved cellular adenoma, the cells being faintly eosinophile.

An important histological feature of these adenomata, a feature which was not sufficiently appreciated by me before review of the entire series was undertaken, is the structural versatility of the group. Some of the growths had an architecture unmistakably like that of the normal gland, so that their recognition was easy. Others exhibited a pronounced network pattern of the epithelial tissue, which somewhat resembled the reticular type of rodent carcinoma (Figure I) and which at first suggested to me that the growths might have arisen from the remains of the stalk of Rathke's pouch, for example, Cases IV and VII. When it was found, however, that similar trabeculation was present in parts of growths which elsewhere had the unmistakable structure of adenomata of the anterior lobe, as in Case XIII, it became clear that these prominently reticular growths were really adenomata. Since this feature is seldom referred to in current descriptions, I have made a special point of it here.

Another feature worthy of note is that some of the growths from non-acromegalic patients nevertheless contained cells with some degree of eosinophile staining properties, for example, Cases II, VI, VII and IX. From such cases it is clear that eosin-staining cells may be present without there being any clinically important degree of hypersecretion of growth hormone. The eosinophile characters of the cells are, however, decidedly less pronounced in the adenomata from non-acromegalic patients than in those from acromegalics.

Adenomata from Acromegalic Patients.

Seven growths were adenomata from acromegalic patients. Six of the seven were from patients who had been treated by operation. The seventh patient was not operated upon, but was subjected to *post mortem* examination. Full *post mortem* investigation of one of the surgically treated cases, number XII, was also obtained. In all cases in this group the growths contained eosinophile cells, the number and intensity of staining of which, however, varied considerably from case to case.

CASE X.—In a male patient, aged thirty-three years, the growth was a well-preserved, strongly eosinophile adenoma resembling the normal gland in architecture.

CASE XI.—The tissues removed from a male, aged twenty-seven years, showed an adenoma, most of which appeared to be chromophobe, but with areas of moderately eosinophile tissue. Much degenerative change was present, including areas of hyaline fibrosis and early calcification.

CASE XII.—The patient, a male, aged forty-two years, was reported by Dr. H. W. S. Laurie, with full *post mortem* study, 1937; and by Dr. L. B. Cox, 1937, Case II. The tumour was a well preserved, strongly eosinophile adenoma with an architecture like that of the normal gland. *Post mortem* examination showed pronounced enlargement of viscera, especially of the heart, which weighed 38 ounces; and death was due to post-operative cardiac failure.

CASE XIII.—In a male patient, aged forty-seven years, the growth was an adenoma, many parts of which had a structure like that of the normal gland, while other areas had a net-like structure resembling that shown in Figure I. Many of the cells were moderately eosinophile. Occasional small patches of calcification were present.

CASE XIV.—From a female, aged thirty-five years, there were obtained fragments of moderately eosinophile adenoma.

CASE XV.—A female patient, aged sixty-seven years, had a strongly eosinophile adenoma with an architecture like that of the normal gland.

POST MORTEM CASE 5302.—A man, aged thirty-six years, was admitted to hospital complaining of loss of weight and strength and persistent vomiting after meals for the previous two months. He died a few days later, and *post mortem* examination disclosed the following abnormalities. The face, hands and feet showed the typical changes of moderately advanced acromegaly. The pituitary fossa was irregularly enlarged to about thrice its normal capacity. Much of the enlarged fossa, however, was empty, the gland occupying only its posterior part. The gland itself was irregular in shape, concave on its upper aspect, thickest posteriorly, and within a thin edge anteriorly and to the right. It was patchily adherent to its fibrous capsule. When carefully dissected out, it weighed 1·7 grammes instead of the normal 0·6 gramme. Microscopically, it contained an adenoma of the anterior lobe, composed of epithelial cells scattered rather sparsely through an abundant connective tissue stroma. Many of the cells were strongly eosinophilic. Scattered foci of calcification were present. Around this adenomatoid tissue a zone of residual normal anterior lobe tissue was present, and there was a gradual transition from the normal to the adenomatoid tissue (Figure II). The thyreoid weighed 90 grammes and contained a small colloid adenoma. The adrenals presented slight general hyperplasia of the cortex, including one rounded adenomatoid mass 1·25 centimetres in diameter. The liver contained two small cavernous angiomata. The stomach was the seat of a diffusely infiltrating, densely fibrous carcinoma of *linitis plastica* type, with an area of ulceration in the pyloric region. Scattered small metastases were present in the peritoneum, and there were large deposits of growth in the upper abdominal, mediastinal and cervical lymph glands.

An important pathological feature of advanced acromegaly, namely, splanchnomegaly, is well exemplified in Case XII. The precise factors responsible for this are obscure, but its practical importance as regards the outlook for the patient deserves emphasis. Long delayed operation may entail the added risk of visceral, usually cardiac, failure, while adequate early operation may avert that risk. The position as regards surgical attack is precisely similar to that in goitres; in both cases, while operation is often called for on account of the local enlargement of the gland itself (with its serious visual results in the case of the pituitary), it may also be beneficial in avoiding dangerous cardiac dysfunction in later stages.

The *post mortem* case detailed above exhibits several features worthy of special note. The first of these is the association of acromegaly with carcinoma of the stomach. Whether or not this was merely fortuitous cannot of course be decided; I

have not been able to discover any previous records of such an association of diseases. A second noteworthy feature of the case is the lack of separation of the adenomatoid and the residual normal tissue (Figure II), a feature which has already been commented on as suggesting that the growth is not a true neoplasm, but rather a hyperplasia comparable with goitrous changes in the thyreoid, a "hypophyseal struma". A third interesting feature of the *post mortem* case was the great enlargement of the pituitary fossa, which, however, was only partly occupied by the enlarged gland. It appears probable that the gland had at some time previously been much larger and had suffered subsequent shrinkage, a view supported by the pronounced fibrous and atrophic changes present in the adenomatoid tissue. Ewing (page 997) cites Huchard's and one of Cushing's cases as instances of acromegaly in which a small sclerosed pituitary lay in an enlarged fossa. Here again we may discern a parallel with goitre, in which also atrophy of glandular tissue, fibrosis, calcification and cystic changes are prone to supervene in the later stages.

Tumours of Doubtful Nature.

Four tumours of the present series are of undetermined origins. They are considered at this stage, however, because in all four instances they may have been epithelial growths arising from the anterior lobe of the pituitary and therefore similar in origin to those already considered.

CASE XVI.—The patient was a female, aged fifty-four years. Complete pre-operative and post-operative clinical details are given by Mr. Trumble. The tissue removed at operation showed an epithelial growth composed of a network of well-defined broad trabeculæ with intervening thin-walled blood vessels (Figure III). The epithelial cells in the trabeculæ were either polyhedral in form or elongated transversely or obliquely in the columns. In most parts the cells were solid in appearance, with darkly staining, slightly basophilic cytoplasm, but in other areas the cells appeared pale and empty, recalling somewhat the structure of clear-celled carcinoma of the kidney (Figure IV).

The general structure of the growth in this case inclines me decidedly to the view that it was a chromophobe pituitary adenoma; in no undoubted renal growth have I ever seen trabeculæ of solid, darkly stained cells like those depicted in Figure III. In view, however, of the presence of areas of pale cells, and of the occurrence of hæmaturia during the post-operative course of the illness, there is a reasonable doubt as to the identity of the growth; it may have been a metastasis of a renal carcinoma.

CASE XVII (and *post mortem* Case 5000).—The patient was a male, aged twenty-six years. *Post mortem* examination revealed a huge irregular growth involving the pituitary region, the adjacent bones, the sphenoid and ethmoid sinuses, the roof of the naso-pharynx, the right superior orbital fissure, and the apices of the petrous bones on either side. The growth surrounded the trigeminal and adjacent nerves, adhered to the anterior parts of the tentorium, and extensively destroyed the affected bones. No remains of the pituitary gland could be found. The optic nerves were thinned and stretched around the lateral sides of the growth. The tumour indented and partly adhered to the floor of the third ventricle and adjacent parts of the base of the brain, but the brain was not invaded. Parts of the growth showed much degeneration and hæmorrhage. No noteworthy abnormalities were found in any of the other viscera. Microscopic study showed a richly cellular spheroidal-celled carcinoma, with scanty stroma (Figure V). The cells were arranged in large irregular masses or in diffuse sheets in the interstices of the residual invaded tissues. In the stromal tissues there were collections of lymphocytes.

The precise origin of this tumour cannot be affirmed with certainty. It may have been a carcinoma of the anterior lobe of the pituitary or of the epithelium of the sphenoidal sinus; in my opinion, its structure suggests a pituitary origin.

CASE XVIII.—The patient was a female, forty-five years of age. Fragments removed from a cystic tumour with a calcified wall showed a highly cellular and vascular growth, consisting of broad perivascular mantles of large tumour cells of uniform structure (Figure VI). The cells had ill-defined outlines, large ovoid or spherical vesicular nuclei, and a moderate amount of basophilic cytoplasm with a fine meshwork of fluffy appearance. Except for the numerous well-formed small blood vessels, the stroma was scanty. Occasional tumour cells were larger than their fellows and contained two or three nuclei. Mitotic figures were few in number. Scattered through the growth were a moderate number of concentrically laminated calcified grains of the "brain sand" or "psammoma" type. These appeared to have formed around small vessels, not in the tumour clumps.

The presence of calcified grains suggested the possibility that the growth was a meningioma, but there was no sign of whorling of the tumour tissue. The general characters of the tumour cells rather resembled those of an epithelial growth, and it may be that the tumour was an adenoma of the anterior lobe of unusual type, or it may have arisen from the Rathke remains.

POST MORTEM CASE 4943.—A female, aged fourteen years, had suffered from amenorrhœa, headaches and lassitude for seven months, and more recently from diplopia, ptosis, complete right-sided ophthalmoplegia, and other signs of destructive basal intracranial disease. The cerebro-spinal fluid was under increased pressure and xanthochromic. X ray examination revealed erosion of the orbital fissures and pituitary fossa. *Post mortem* examination revealed no relevant abnormality of any of the thoracic or abdominal organs. Facio-cervical viscera were normal, except for pronounced enlargement of lingual and faucial tonsils and a large mass of post-nasal adenoids. The pituitary region and its environs were the seat of a soft, friable, hæmorrhagic, infiltrating growth. The fossa was enlarged to double its normal size and filled by growth; no residues of the pituitary gland could be found. The growth had occluded the cavernous sinuses and extended diffusely outside the dura into the orbital fissures, the floors of the middle fossæ of the skull on both sides, and into the posterior part of the right orbit. In all these areas the bones were eroded and partly replaced by soft growth, which extended also into the sphenoidal sinus. The tumour had also massively invaded the base of the brain about the optic chiasma and interpeduncular area. The third ventricle was filled by growth, which also occupied both foramina of Monro and part of the left lateral ventricle, and extended within the iter to the anterior angle of the fourth ventricle. There were no implant tumours in the ventricles or meninges. There was pronounced internal hydrocephalus of the lateral ventricles. Microscopically the tumour consisted of a highly cellular, largely diffuse and disorderly tissue composed of large spheroidal or rounded cells with pale cytoplasm, large nuclei and many mitotic figures. Strands of stroma were sparsely scattered through the diffuse

cellular growth, and these showed collections of lymphocytes. This feature and the large pale cells of the growth itself formed a histological picture resembling that of seminoma of the testis in many parts (Figure VII).

The origin of the growth remains in doubt. It may have been of a kind similar to that of Case XVII, but more rapidly growing and anaplastic; and it may therefore have been a carcinoma of the pituitary gland or of the sphenoidal sinus. The tumour tissue was, however, so undifferentiated and diffuse in this case that it was impossible to be sure even that it was epithelial in origin.

Tumours Derived from Remains of Rathke's Pouch.

Since the publication of the classical work of Erdheim on pituitary tumours there has been general recognition of a group of growths which arise from Rathke's cleft or from the epithelial remnants of the stalk of Rathke's pouch. A useful recent summary of the subject is given by Frazier (1936). Two of the growths in the present series belong to this group. One of these was an "adamantinoma", the other a cyst lined by cornifying squamous stratified epithelium.

Adamantinoma.

CASE XIX.—The patient was a female, aged fourteen years. Fragments of tissue removed at operation from a large cystic growth exhibited the characteristic structure of "adamantinoma", as shown in Figures VIII and IX. The epithelial clumps showed marginal columnar cells forming a palisade, and central areas of stellate and frayed cells forming a loose network with large intercellular spaces. Many of the epithelial clumps contained patches of cells with squamous characters and cornification, in some parts forming prominent laminated masses of keratin. Patchy calcification was present in the growth, particularly in the older masses of keratin. The clumps of epithelial tissue were set in a stroma of typical neuroglial tissue, the identity of which was established with certainty in sections stained by Heidenhain's iron-hæmatoxylin and van Gieson's stains. The patient died a few weeks after operation.

Post mortem examination (Austin Hospital) revealed a large partly cystic growth, 4·5 centimetres in main diameter, occupying the pituitary area and region of the third ventricle, which was occupied and almost occluded. The optic chiasma and tracts were stretched around the anterior and lateral aspects of the tumour. The brain-stem was not invaded, but was displaced backwards, so that in the mid-line the distance between the chiasma and the posterior angle of the interpeduncular fossa was 4·5 centimetres. The growth bulged slightly into the foramina of Monro, but did not extend into either of the lateral ventricles nor into the iter. Microscopically the structure of various parts of the growth was similar to that already described. In many places the epithelial clumps lay in neuroglial tissue, and at the upper borders of the growth the clumps could be seen invading the nervous tissue near the optic chiasma and in the neighbourhood of the fornix. The peripheral parts of the tumour showed the "adamantinoma" structure best; the central areas exhibited much cornification, cystic degeneration, and patchy calcification, especially of the cornified material.

Squamous Epithelial Cyst.

CASE XX.—The patient, a male, aged twenty-seven years, was described by Dr. L. B. Cox, Case IV. At operation some fluid was aspirated from a cyst, the wall of which was then removed. Microscopically this was lined by stratified epithelium with cornification, desquamation and partial calcification of its inner layers. Outside the cyst there was a small amount of altered anterior lobe tissue.

Most of the growths arising from the remains of Rathke's pouch take the form of epidermoid carcinomata or cysts, and many of the solid growths show close structural resemblance to "adamantinomata" of the jaws. Several of the terms used in describing this group of tumours are open to objection. The name "craniopharyngioma", which has been applied to the whole group in order to denote its origin from the Rathke stalk, is not only a clumsy word, but, like the name "craniopharyngeal duct" itself, it fails to remind us that Rathke's pouch is developmentally an oral outgrowth. The term "adamantinoma" also is objectionable, since it implies an origin from enamel-forming epithelium. This assumption is almost certainly false both as regards the tumours of the jaws and those of the pituitary region. There is no valid reason for believing that the epithelial residues of Rathke's stalk have dental potencies; and, granted that the "adamantinomata" of the jaws do arise from the remnants of the dental lamina, these remnants themselves do not normally have enamel-forming powers, since they do not form any enamel. Only the epithelium of the tooth germs is enamel-forming. The tumours of the jaws and pituitary region to which the name "adamantinoma" is applied are best looked on as growths of the epithelial remains of developmentally early oral evaginations, remains which normally persist in these two regions and which possess no special potencies for differentiation. This view resolves the difficulties of explaining why "adamantinomata" should occur in the pituitary area where no dental epithelium exists, and why "adamantinomata" in any situation never actually form any enamel. It is, however, not surprising that tumours derived from oral epithelium should exhibit squamous-celled differentiation as seen in "adamantinomata" (Figure IX) as well as in the other epidermoid growths of this region.

Fibrosarcoma of the Pituitary Region.

The following case is recorded in some detail both on account of the peculiar clinical history and diagnostic difficulties, and the unusual pathological findings. I have not been able to discover any records of similar cases.

POST MORTEM CASE 5315.—A male patient, aged sixty-seven years, was first admitted to the Alfred Hospital in November, 1936, under the diagnosis of "*tabes dorsalis* and possibly gastric syphilis". In 1924 he had suffered from impaired vision, general weakness and pains in the back and limbs; his blood was said to have given a positive reaction to the Wassermann test, and he was given anti-syphilitic treatment for the next six years. At the end of this time he felt well, his response to the Wassermann test was said to have been negative, and treatment was discontinued. He then remained well until eighteen months prior to his admission to hospital, when he began to feel weak, to lose weight and to suffer from indigestion. Six weeks prior to his admission to hospital he had a sudden fainting attack, vomited some dark fluid and passed tarry motions for several days. He was admitted to hospital under the diagnosis of "*tabes dorsalis*, ? gastric syphilis". Without full details of all neurological and special findings being given, suffice it to state that these,

though not fully typical of *tabes dorsalis*, were considered by the clinicians as compatible with that disease. The Wassermann test, however, gave negative results in both blood and cerebro-spinal fluid, and the latter was microscopically and chemically normal. The readings of the Lange colloidal gold curve were 0122100000. Occult blood was present in the fæces from time to time, and skiagrams of the stomach following a barium meal showed prepyloric narrowing suggestive of an organic lesion "consistent with gastric syphilis". A test meal showed high acidity. While in hospital he rapidly became blind in the left eye, which became œdematous and showed signs of atrophy. A course of tryparsamide and "Bismol" injections was given, and the patient was discharged in December under the diagnosis "*tabes dorsalis*, gastric syphilis".

He was readmitted on February 16, 1937. The left eye was more severely diseased and had undergone proptosis. Blood and cerebro-spinal fluid still failed to react to the Wassermann test, and the cerebro-spinal fluid was normal. The Lange readings were 012210000. The patient became very depressed and spoke of suicide. He was discharged from hospital on March 29 under the diagnosis "*tabes dorsalis*, blindness, gastric syphilis". A few days before his discharge a small raised mass was noticed projecting from the right frontal bone; this was thought to be a gumma of the skull. He was admitted to Mont Park Mental Hospital on April 1, after attempted suicide. Here he received a course of malarial therapy, though there were no definite signs of *dementia paralytica*. On April 8 blood and cerebro-spinal fluid failed to react to the Wassermann and Vernes tests, and the cerebro-spinal fluid appeared normal. He was transferred to the Alfred Hospital again on April 29 under the diagnosis "syphilitic panophthalmitis". The left eye was protruding and infected, and the mass on the skull had increased in size. The patient died on May 1 and, prior to *post mortem* examination, the causes of death were entered as "neuro-syphilis, *tabes dorsalis*, panophthalmitis".

Post mortem examination revealed a huge, densely fibrous, hard, white growth, which largely replaced the basi-sphenoid, ethmoid, roof and medial wall of the left orbit; which occupied the pituitary region where it surrounded and compressed some remains of the pituitary gland; and which extended into the roof of the pharynx as projecting lobules of growth. It invaded the bases of both frontal lobes, the optic chiasma and floor of the third ventricle; and pressed into but did not invade the brain-stem. The left eye was thrust forward and almost completely disorganized, clearly as a result of the destruction of all the retrobulbar structures by the growth. The lungs contained many hard white spherical metastatic growths up to two centimetres in diameter, and there were multiple metastases in the calvarium. No metastases were found in any other viscera, lymph glands or bones. The liver showed a moderate degree of cirrhosis.

Microscopic examination revealed spindle-celled fibrosarcoma, most of which was densely fibrous and poorly cellular. The parts of the growth invading the brain, however, were fairly richly cellular, as were also the metastases in lungs and skull. In the pituitary region the growth contained calcified granules, but whorled arrangement was nowhere present and there was nothing to suggest meningiomatous characters. The precise site of origin of the tumour remains undetermined.

The *post mortem* findings in this case make it clear that all of the symptoms and signs of the final illness, which were attributed clinically to syphilitic disease of the nervous system, were really due to the tumour. It was a remarkable coincidence that, in a patient who had a strong history of previous syphilis, a rare tumour should have arisen in a situation where it could produce changes in ocular reflexes, optic atrophy and other neurological abnormalities suggesting neuro-syphilis.

Summary.

1. Sixteen examples of pituitary adenomata are described. Many of these growths appear to be not genuine tumours, but hyperplasias or "strumas" comparable with goitre. They present a wide range of structure, a prominent retiform mode of arrangement being particularly apt to cause difficulty in histological identification. All growths from acromegalic patients in this series contained eosinophile cells, but faint eosinophile characters were seen also in some of the growths from non-acromegalic patients. The risk of splanchnomegaly with cardiac failure in cases of long-standing acromegaly is an added reason for early operation in this disease. One of the patients in this series suffered from both acromegaly and carcinoma of the stomach.

2. Four tumours of uncertain nature, possibly arising from the epithelium of the anterior lobe, are described. Two of these, both studied completely *post mortem*, were highly cellular malignant growths with wide invasion and destruction of the basal tissues and bones of the skull.

3. A case of "adamantinoma" and a case of squamous epithelial cyst of the pituitary are described. The names "adamantinoma" and "craniopharyngioma" are criticized.

4. A case of fibrosarcoma of the pituitary region, with metastases in the lungs and vault of the skull, is described. Clinically the illness had been regarded as due to neuro-syphilis, and the tumour was not suspected until discovered *post mortem*.

Acknowledgements.

I am indebted to Mr. H. C. Trumble for details of the cases in which surgical operation was performed, Dr. L. B. Cox for valuable help in histological diagnosis and description of the tumours, and to Dr. W. S. Newton for permission to refer to the clinical details of the last case.

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Legends to Illustrations.

FIGURE I (Case VII). The microscopic appearance of the retiform structure in adenomata. × 200.

FIGURE II (*Post Mortem* Case 5302). Photomicrograph showing gradual transition from the adenomatoid tissue *X* to normal anterior lobe tissue. × 42.

FIGURE III (Case XVI). Microscopic appearance of the darkly staining epithelial trabeculæ of the growth. × 42.

FIGURE IV (Case XVI). An area of the growth showing pale cells. × 200.

FIGURE V (Case XVII). Photomicrograph of the highly cellular spheroidal-celled growth. × 85.

FIGURE VI (Case XVIII). Microscopic structure of the growth, showing perivascular mantles of cells. × 85.

FIGURE VII (*Post Mortem* Case 4943). Highly cellular anaplastic tumour with lymphocytes in its stroma. × 85.

FIGURE VIII (Case XIX). Characteristic "adamantinoma" clumps invading neuroglial tissue. × 85.

FIGURE IX (Case XIX). "Adamantinomatous" clumps, with an area of early squamous-celled differentiation, shown by the arrow. × 85.

THE ROLE OF THE SMALL INTRACRANIAL BLOOD VESSELS IN THE PATHOLOGY OF BRAIN CONDITIONS.[1]

By OLIVER LATHAM, M.B., Ch.M.,
Pathologist to the Department of Mental Hospitals, Government of New South Wales.

THE neuro-pathologist receives many brains with no spectacular lesions nor visible diseased blood vessels. I refer specially to brains and cords which, on further histological examination, are found to contain nothing more than œdema, *status spongiosus* and maybe more or less affection of the small blood vessels. Not always are we happy in making definite diagnoses about degenerated neurones in slides of this sort. Of course a more elaborate pathological picture may present itself. When, therefore, I was asked for a paper, I thought I should put down my "reactions" to these problem brains; and since then I note that both overseas and here cerebral arteriosclerosis has come much to the fore. Working with Professor Dawson, I carefully reexamined most of our old specimens received during the last twenty-five years and thus branded, and I must admit that in the light of more recent knowledge much more was recognized in them. I must add that the report "a diseased state of the small blood vessels" is not always considered adequate by clinicians.

It was my good fortune to spend some time in Ford Robertson's laboratory, because in 1896 this observer proved in striking manner the fundamental truths of Gull and Sutton's great work (1872) on fibrohyaline degeneration of the small blood vessels, especially (and more correctly) the arterioles and capillaries of the pia-arachnoid and the cortex. Many neuro-pathologists since then have devised their own experiments to reproduce these lesions in animals in order to study the various stages in the process, and all stress their great importance.

Again, it would appear the fashion today, rightly or wrongly, to implicate errors in the circulation when the ætiology of many apparently diverse pathological brain and cord findings is being sought.

Some Physiological Factors Concerned.

Much confusion has obtained in endeavours to disclose the most typical picture of brain states in vascular failure. This is partly to be accounted for by the different stages of the same process encountered, partly by the newer stains revealing glial cells and young mesenchyme not previously known, and partly by the apparently opposite pictures of fairly sound vessels with damaged neurones and also damaged vessels (in patients accidentally killed) with fairly good neurones when no symptoms have occurred during life. Again, we may have wet and dry swollen brains, and the curious phenomena of œdema and red-cell diapedesis from apparently healthy vessels on a wide scale, or distant from the site of an injury. Krogh and his co-workers began to show the independent capacity of the capillaries of the skin and other tissues to contract and dilate, not only severally and independently amongst themselves, but also quite independently from the arterioles *et cetera*. He found as much as 700 times more blood in the working muscles than in the resting muscle, and he found that heart muscle might have 2,700 capillaries per square millimetre. Ordinarily, all capillaries would not be open or visible together; but in the brain all were so, although of course not dilated to full capacity. Quite a number of facts became known, such as the increased permeability of capillaries when dilated. Particles like (soluble) starch granules, five microns in width, could then pass out of the dilated capillaries. In somewhat similar states so could serum, and the red cells would be left too concentrated and agglutinated. Thus, not only might irregularities in the circulation be set up, but the red cells might be permanently damaged. The way would thus be paved for stasis and prestasis, terms which throw light on some histological pictures. If things had not gone too far the tissues might recover, and the process was said to be reversible. If the experiment or diseased state was prolonged too far, the process became irreversible; and we know that shutting off the blood supply to the brain for a minute results in an irreversible state, the neurones being permanently damaged. Crile, among others, shows very clear pictures of these states.

Substances were found which, on injection or mere application to the vessels, produced dilatation or contraction of the small blood vessels, or such paralysis of the capillaries that the dilated little vessels allowed maximum permeability. The discovery of vasomotor nerves on the intracranial blood vessels now added another factor to be reckoned with in this discussion.

The Small Cerebral Blood Vessels.

Robertson's simple description of the small cerebral blood vessels always appealed to me. A capillary would be a simple tube of endothelium which, on pushing its way through the pia into the cortex, would carry with it a sleeve of the pial fibres, the smallest only a fibre or two, yet providing perivascular spaces. It is this fibre that is so prone to fibrohyaline degeneration. The endothelium has its own forms of reaction. For a larger arteriole, imagine a greatly increased fibrous coat, in the middle zone of which small muscle fibres, mostly circular, entwine themselves. The few elastic fibres usually present within this muscular layer now become the important internal elastic lamina, and the fibres between the elastic lamina and the endothelium are called the subendothelial layer, and it is here that hyaline changes first start. The fibres outside the little muscles become the adventitial coat and the contained spaces become the Virchow-Robin spaces. The expanded feet of the glia cells on the outermost fibres constitute

[1] Read at the fifth session of the Australasian Medical Congress (British Medical Association), August, 1937.

the fibro-glial membrane, one of the barriers through which, in a healthy individual, but few cells should penetrate. In the course of this paper I propose to show examples of hypertrophy and/or degeneration of the fibro-glial membrane and of the adventitial coat, whether by new or older fibres, and dilatation and packing of the Virchow-Robin spaces, granular degeneration of the media, splaying of the elastic lamina, early changes in the subendothelial region, and proliferation or toxic swelling and degeneration of the endothelium.

Intravascular stains can penetrate far into the media; hence we can realize that toxins or malnutrition from metabolic diseases like kidney and liver trouble, lead and alcohol poisoning, and acute infective states like pneumonia, may affect the inner coat; while breaking down of neurones can produce compounds which must traverse the adventitial spaces, causing first proliferation and then degeneration of the fibres, as well as filling *Gitterzellen* with altered myelin which must reach the pia this way. Hence infections like syphilis and *encephalitis lethargica* may cause vascular reaction, both by their presence in the vessel wall and by their indirect effects on neurones. Calcarious sand in the capillaries encourages further examination and, as Wertheim warns us, we must carefully distinguish thickening of a vessel's coat by invasions of cells from true proliferation of the cells of the wall.

At times small vessels may become solid hyaline bars, and even then the endothelium may persist. Commonly the new capillaries called into being are grossly dilated and rupture easily. Sometimes rings of red cells may surround what look like sound little vessels. After such items as these have been noted, the tissues about these vessels are searched for glial changes, microglial phenomena, and the presence of endothelial cells, plasma cells, polyblasts, lymphocytes and polymorphonuclear cells outside the vessel lumens and in the Virchow-Robin spaces or brain tissue proper. The presence of some of these cells, even when the vessels look normal, surely points to nutritional failure of some sort, and indicates that the myelin is not healthy. On other occasions little areas or cysts may be discovered, crammed with *Gitterzellen*; or just previous to this may be found parallel lines of rod cells or, a little later, minute, wedge-shaped infarcts with syncytial glia or true fibroglial cells bridging across the old cyst. If larger, one can see with the naked eye the so-called *état criblé*.

Patients with kidney disease or with general paralysis of the insane, who have fits of confusion, recover many times and at last die, show these glia and invading cells in areas which were waterlogged, and managed to recover. Stanley Cobb mentions a type of case in which the patient suffered from right-sided Jacksonian epilepsy, ending in *status epilepticus* and death. Autopsy revealed no softening or gross brain lesion; but slight pallor of the left cortical motor area and ischæmic or early anæmic necrosis of the nerve cells were found. Hard and dry swollen areas must be distinguished from local œdema, a state often found in sections from brains sent to our laboratory, and which interferes with staining reactions and the making of good sections.

The Conception of Vasomotor Control of the Small Blood Vessels in the Brain and Cord.

Once the intracranial blood vessels were shown to possess vasomotor nerves, it was an easy step to postulate functional derangements of blood vessels sufficiently intense and prolonged to cause necrosis. Experiments and clinical observation took a new turn in view of these facts. Injuries, surgical shock and emotional "turns" might be proved capable of such an effect on vascular tone. First simple chemicals, then organic drugs, and finally products of metabolism or extracts from damaged areas were used. Cerebral extracts, adenosine, phosphoric acid, histidine and tryptophane (all vaso-dilator) caused cerebral hæmorrhage when injected into guinea-pigs; on the other hand, glycocoll, tyrosine and leucine (vaso-constrictors) did not. Some of these substances are such as develop in the brain weeks or even months after accidents, and may account for late cerebral hæmorrhage.

The Application of Vascular Tone Effects to the Elucidation of Brain Lesions and of Clinical Phenomena.

In the words of Hiller and Grinker: "In neuropathology the pathogenesis of many lesions otherwise difficult of comprehension may be more easily explained as caused by functional disturbance of the nervous system than by organic causes." G. Richer has shown that slight stimuli to the vasomotor nerves result in vascular dilatation followed by acceleration of the blood stream. Stronger stimuli cause vaso-constriction followed by dilatation of the capillaries, and when they are accompanied by a slowing of the circulation, prestasis with petechiæ usually occur. Local stasis may develop, and if it does so rapidly, it may lead to agglutination of the red cells. A stasis is reversible and is not accompanied by transudation of serum; whereas a prestasis with retardation of the blood stream (as in inflamed states) is associated with transudation; then red-cell diapedesis results, especially near necrotic areas. By application of these principles to the brain the lesions of carbon monoxide poisoning there can be explained on a circulatory basis, as well as some brain states in eclampsia and pertussis. Richer holds that the same is true for epileptic phenomena of some kinds, and von Braunmühl thus explains some cases of mania and puerperal insanity.

Some Experiments Reproducing Brain Lesions.

Winkel and Eckel by injections into blood vessels produced many pictures, endothelial as well as general hyperplasia, such as may be seen in *lues* and also in certain types of food poisoning. Heubner with gold salts got great vascular dilatation with hæmorrhage. Orr and Rows, who did so

much to clarify our ideas about hæmatogenous and lymphogenous reactions, used similar methods, and with ingested germs or India ink, or increasingly strong solutions of argyrol produced brain reactions different in each case. The stronger injections produced irreversible, incurable effects, such as great capillary dilatation and œdema, which latter interfered with the flow of the capillaries at their anastomoses. They agree with Cobb that the capillaries rather than the larger vessels anastomose in the cortex, to a less extent in the central nuclei, and least of all in the hippocampus, where as a result most damage obtains. Experiments allowing a pull to be exerted on the blood vessels supplying the brain and presumably causing a long-continued and severe nerve irritation seemed to cause much worse damage than mere compression of vessels, ten minutes of such pulling causing most severe neurone damage and all kinds of glial and interstitial reactions. Toxins, too, can produce irritation, such as are produced by crushing limbs or burns; for shock does not eventuate while the crushed limb is kept clamped. The severe lesions (axonal degeneration of neurones) that occur when glancing bullets strike spine or occiput, or when boils *et cetera* affect nearby tissues, and which used to be put down to effects on "nutritional nerves", may now be laid at the door of circulatory disturbance; so may also apparently those temporary spinal paralyses taking place when tigers and horses are similarly hit. Reichel and Mathes, endeavouring to explain regional ileitis, injected sclerosing fluids into the lymphatics of dogs' intestines, with corresponding pictures. Nature seems to do something like this when she runs toxic cerebral fluid through the adventitial spaces and the pia.

Finally, by examination section by section of the areas surrounding a bullet wound in the brain till the furthest part affected is reached, it is found that the proximal area is œdematous and non-staining, the next zone contains perivascular hæmorrhage and damaged brain, while the most remote contains small hæmorrhages round the capillaries and ischæmic changes in the ganglion cells. Trotter speaks about unresolved contusions, and we have also to recognize that neurones may undergo necrosis and the area containing them appear as if they had just dropped out; and of course there are certain forms of psychoses which are associated with primary neuronic degeneration.

An Explanation of Sudden and Widespread Petechial Hæmorrhages.

The rupture of an aneurysmal or other defect in a large intracranial vessel and the result produced can be readily understood. Not so easy of comprehension are those cases wherein innumerable widespread petechiæ occur apparently at the same moment; I exclude for the moment those occurring in capillaries in acute infectious diseases.

I recall a case in which a young maidservant had a death stroke. The autopsy revealed both ventricles to be filled with blood, apparently from a ruptured small vessel beneath the ependyma of the lateral ventricle. There were, besides, widespread petechiæ and long-standing fibro-hyaline degeneration of the arterioles and capillaries. In another case a young man fell onto his head, suffering some headaches and increasing failure of vision for about seven weeks and then had a sudden stroke. Here, too, the autopsy revealed innumerable hæmorrhages or, rather, what appeared to be patches of bleeding; yet the most careful histological examination failed to reveal a diseased vessel, and the whole picture was due to multiple petechial hæmorrhages from capillaries.

Hassin suggests one explanation. His patient had hypertension and died from a ruptured aneurysm of the left perforating artery. The extensive basilar hæmorrhage that followed caused a fall of pressure in the parent artery (internal carotid) and thus in the middle cerebral artery. This was necessarily followed by a sudden rise in the corresponding veins, which were diseased. The numerous diseased veins in the ipsilateral basal ganglia could not adapt themselves to the sudden change of blood pressure, and so multiple hæmorrhages came about, although the diseased veins could carry on under ordinary states.

In another case of mine a youngish man with a history of kidney trouble and recent attacks of giddiness and confused states fell off a ladder and died within a day or so. *Post mortem* examination revealed some probable softening or œdema deep in the left parieto-temporal area. The large blood vessels were quite sound, while the capillaries and small arterioles were severely diseased. Innumerable hypertrophied glia and adventitial cells among the poorly-staining myelin showed that this œdematous part had long suffered from malnutrition.

This was a good example of Biggart's dictum: "The naked eye appearance of the larger vessels is no criterion of the presence or absence of vascular damage."

Some Notes of Cases Wherein Diseased Small Blood Vessels Have Played a Part.

Quite a number of lesions of pia, blood vessel, neurone and glia, as well as the presence of amyloid bodies, of invading cells, of blood cells and of granules like hæmatoidin, and excess of iron and lime *et cetera*, can be proved or suspected by the use of hæmatoxylin and eosin stain, by embedding in paraffin and by the making of a frozen section. Of great importance is von Braunmühl's silver stain for young mesenchyme fibres in the vessels, which also shows up Alzheimer's senile plaques. Gold sublimate and our special Nissl technique are used for normal and altered neurone and glia. Myelin, Van Gieson and Marchi's preparations are often useful, together with one of the fat stains, such as Sudan IV. It is rather by careful comparison of all the lesions noted that we can arrive at some sort of diagnosis, always remembering the value of a careful history-taking and a consultation with the clinician. When but little can be seen we must look for evidences of functional vascular failure. The brain, too, must be considered in reference to conditions obtaining in other parts of the body, to its age and to the time factor.

Professor Lambie asked me to make sections of the brain of one of his patients who had died of renal disease, and I found numerous microscopic softenings and cal-

ILLUSTRATIONS TO THE ARTICLE BY DR. HUGH C. TRUMBLE.

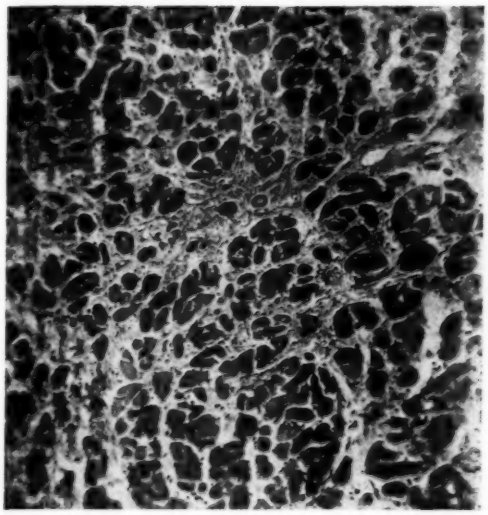

FIGURE VI.

Photomicrograph of the heart muscle of a patient (Case XII) with gross acromegaly, showing advanced degenerative changes. The heart weighed 38 ounces.

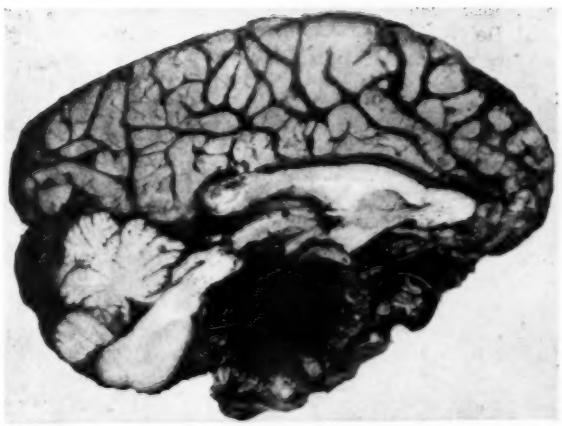

FIGURE VII.

Photograph to show huge invasive tumour at the base of the brain, probably originating in the pituitary gland (Case XVI). The growth is larger in section than the cerebellum.

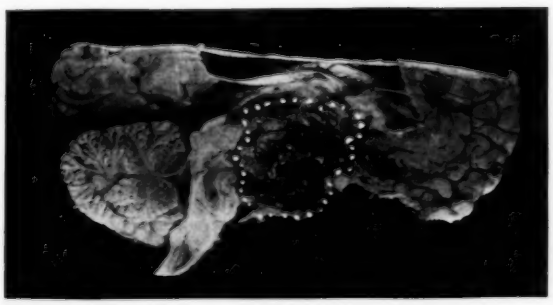

FIGURE VIII.

Photograph of the brain obtained at *post mortem* examination (Case XIX) to show a partly solid, partly cystic tumour almost filling the third ventricle. The tumour shows the structure of an adamantinoma.

ILLUSTRATIONS TO THE ARTICLE BY Dr. RUPERT A. WILLIS.

Figure I.

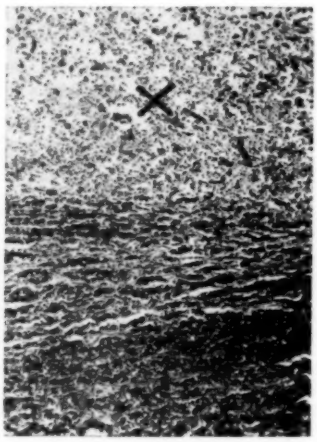

Figure II.

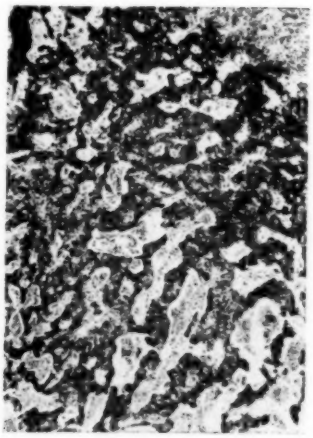

Figure III.

Figure IV.

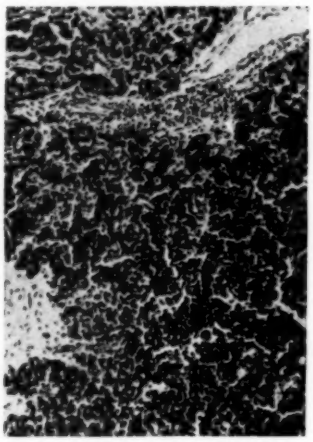

Figure V.

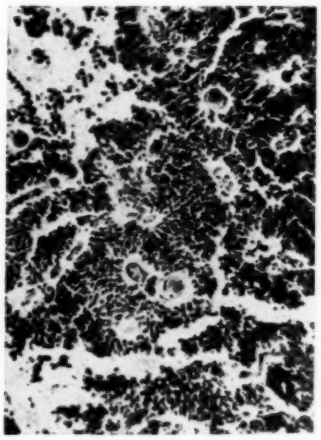

Figure VI.

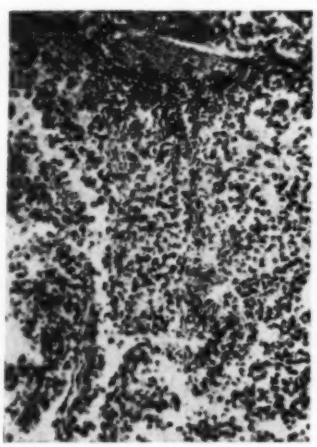

Figure VII.

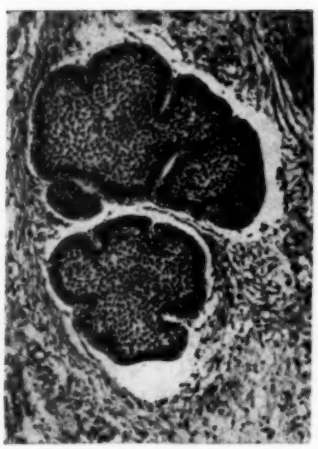

Figure VIII.

Figure IX.

ILLUSTRATIONS TO THE ARTICLE BY Dr. OLIVER LATHAM.

Figure I.

Figure II.

Figure III.

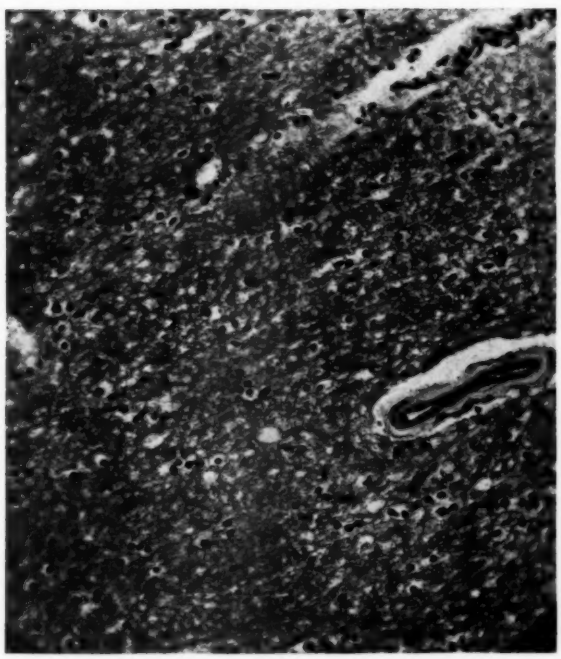

Figure IV.

ILLUSTRATIONS TO THE ARTICLE BY DR. OLIVER LATHAM.

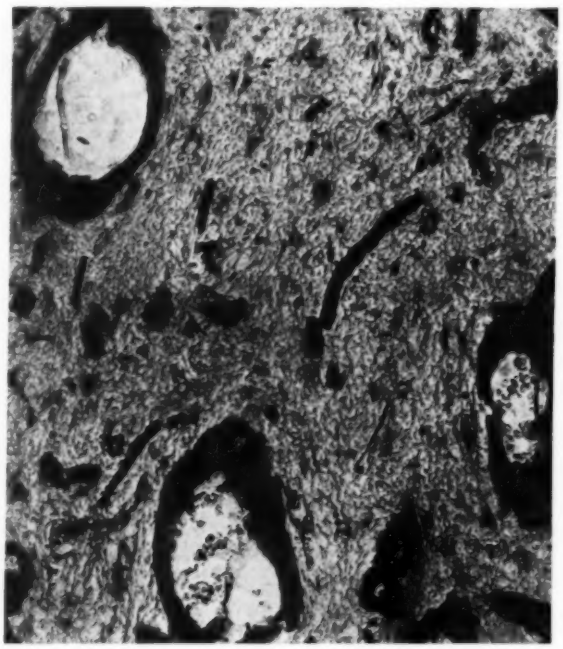

FIGURE V.

FIGURE VI.

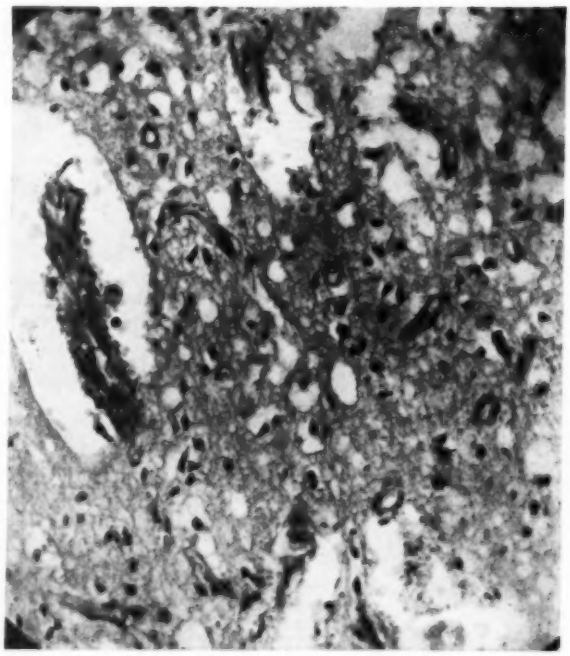

FIGURE VII.

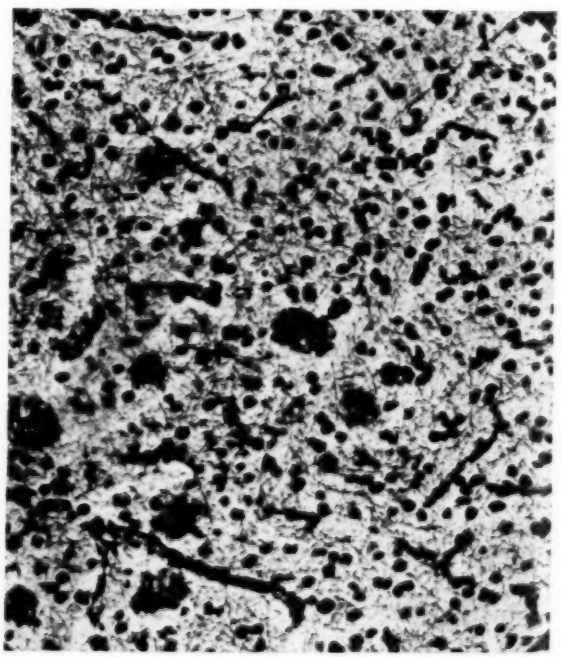

FIGURE VIII.

careous capillaries. In an atrophic dement's brain, close by larger vessels which were normal, alternate wedge-shaped infarcts were noted in the cortex. Examination of a chronic epileptic's brain with cyst-like cavities disclosed extraordinary hyaline degeneration of the small vessels, the pipes having become solid opaque bars; yet even in some of these the endothelium persisted. Calcareous capillaries were also noted in the following three cases: (*a*) in the cortex and cerebellum of a patient who had died of lead poisoning, (*b*) in a case of *encephalitis lethargica*, and (*c*) in the dentate nucleus of a young married woman, with signs of acute confusional psychosis, who recovered consciousness three times in her illness of ten days' duration. Further prolonged search revealed many *Gliarasen* in her central nuclei, and obvious signs there of vascular stasis and neurone destruction. If this was an infection, the question arises: Does infection cause a lethal issue by producing a stasis or prestasis? Examination of the whole brain of an old man who, however, was in a good position but deteriorated rapidly, revealed almost wholesale atrophy of his supporting neuroglia, the neurones being separated by homogeneous masses. A child, aged six years, with clinical signs including rheumatic endocarditis, had both ventricles distended with blood and a small area of softening near by. Hyaline arterioles were plentiful, and the first cortical layer seemed to escape. Frequently specimens used to be sent labelled "*encephalitis lethargica*". One such, from a woman aged twenty-eight years, contained acute degeneration of the capillaries, which apparently produced millions of microscopic softenings in and just below the first cortical layer, with *Gitterzellen*. The history also included septic pneumonia, and I wonder whether this caused the capillary failure.

Examination of the brain of a child dead of a "mysterious disease" revealed widespread productive arteritis of the small vessels in the cerebellum as well as microscopic softenings and *Gitterzellen* and areas of fibrous gliosis. Food poisoning was suggested as a cause. Two cases of *encephalitis lethargica*, one of Korsakoff's disease and one of "X" disease presented peculiar affections of groups of end capillaries, leading to obvious neurone destruction. Four cases of *lues* in various stages presented, respectively, rod cell production with slight endothelial proliferation, the same much increased, early productive arteritis and toxic thickening, and general paralysis with the great capillary hypertrophy in the first cortical layer. A mental patient like the last, with no reaction to the Wassermann test, presented the same histological picture. A boy aged eight years, dead of a fit, had arteriosclerosis of some degree in his cortex. There was nothing specific in its appearance, but granulations in his aqueduct and ventricles suggested congenital *lues* and a congestive attack. Acute encephalitis can quickly affect small vessels, and a case of subacute mania shows well the intense congestion of the third cortical layers. Finally, a child's cerebellum was sent to me to discover why one dentate nucleus area was twice as large as in the other hemisphere; tumour was suggested. The histological examination revealed plasma cell reaction and hyaline vessels on both sides; and in the larger hemisphere progressively increasing supporting glia degeneration, vascular prestasis with altered blood cells, and obvious neurone degeneration from one side of the dentate nucleus to the other could be traced. The swelling was explained on a circulatory basis.

Acknowledgements.

I have to acknowledge my indebtedness to Mr. Hedger, our chief technician, for the sections, and to Mr. L. Schaeffer, of the Department of Anatomy, for the photomicrographs.

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Legends to the Illustrations which will be found on the Special Pages.

FIGURE I. While the blood vessel below, about 0·5 millimetre in thickness, seems fairly healthy, yet the capillaries and arterioles (represented by longitudinal aggregations of black dots) are quite calcareous, and in fact are associated with definite infarcts. Diagnosed artriosclerosis.

FIGURE II. This shows two vessels in the caudate nucleus, cross section of the larger revealing fibrohyaline degeneration. The walls of the smaller, a small arteriole, are thickened by proliferation of cells in all walls. There were many microscopic infarcts.

FIGURE III. A thickened vessel separates two fields of the microscope. The normal right field contains healthy regular neurones, the left contains an infarct. The syncytial glia can be seen replacing the nobler elements, yet there is not much disturbance of the parts. The ground tissue stains as usual.

FIGURE IV.—This is taken from a young man who died of chronic nephritis; he had mental confusion and fits, and death occurred rather suddenly. The major intracranial blood vessels were healthy. Intense fibrohyaline degeneration is seen in the small vessel (on the right of the picture), and proliferation and degeneration of the adventitial wall are seen in the capillary (top right). Definite degeneration of the neuroglia of the whole area (most of the temporal lobe) is seen, bespeaking long-continued malnutrition, œdema and stasis.

FIGURE V. This is from a male, aged about thirty-five years, who died of chronic nephritis. Intense fibrohyaline degeneration of the blood vessels less than 0·5 millimetre in width is seen, yet the endothelium is often preserved. Some of the arterioles and capillaries (middle of picture) are just solid bars of homogeneous material. There were many macroscopic cysts in the brain, in types of infarcts.

FIGURE VI. This is from a case of sudden mental failure leading to hopeless dementia in an old man in good position, and shows extraordinary homogeneous degeneration of the neuroglia (here in the olives), in the grey matter and round vessels all through the brain. It is important because in a less degree this feature would point to malnutrition of some standing in the suspected areas.

FIGURE VII. This is from a case of brain syphilis (not general paralysis). The proliferated endothelium causes vascular blockage (seen in the vessel on the left) and innumerable microscopic hæmorrhages (bottom right) and œdema. Many minute areas of softening obtain, and *Gitterzellen* can be seen near the larger vessel on the left. A similar result may eventuate from toxic swelling of the endothelium of these artrioles and capillaries in pneumonia and suchlike infective states; it should be remembered, however, that the lesions themselves may be sterile, that is, no germs may be present at the spot.

FIGURE VIII. A section from the brain of an old man submitted for examination from the Royal Prince Alfred Hospital. Von Braunmühl's silver reaction brought out quite unexpectedly numerous senile plaques (the circular bodies) and young argentophile fibres on the small blood vessels. These structures, not revealed by the usual stains but brought out by silver, suggest malnutrition on a vascular basis—that is, failure of the small blood vessels to function, although the larger vessels were healthy.

THE RICKETTSIA OF "Q" FEVER: FURTHER EXPERIMENTAL STUDIES.[1,2]

By F. M. BURNET and MAVIS FREEMAN.
(From the Walter and Eliza Hall Institute, Melbourne.)

IN a previous paper (Burnet and Freeman, 1937) the association of Rickettsiæ with the infection produced in animals by the agent of "Q" fever (Derrick) was reported. Only one strain of virus was used in this work, and although we felt that the evidence was reasonably conclusive that the Rickettsiæ represented the ætiological agent of the disease, certain reservations were made.

The present paper reports additional findings, particularly in regard to the use of agglutinating emulsions of Rickettsiæ, and is considered to provide final proof of the ætiological importance of the Rickettsia. Throughout we have had the fullest cooperation of Dr. E. H. Derrick, who has kindly supplied all the human blood and sera to which reference is made, as well as providing the relevant clinical data.

Direct Isolation of Rickettsiæ from Patient's Blood.

Blood clot from the patient "Joh.", taken on the fifth day of illness, was received by plane about twenty-nine hours after it had been obtained. The clot was ground with quartz powder and a little nutrient broth and lightly centrifuged, and the supernatant fluid was inoculated intraperitoneally into six mice. Two died of bacterial infection. Of the others, two killed on the tenth day had no splenic enlargement, and no Rickettsiæ were noted in spleen smears. The remaining two were killed on the thirteenth day. One had an enlarged spleen (19·0 by 6·5 millimetres), and Rickettsiæ were seen in the smear; the other had a small spleen, but the smear revealed numerous Rickettsiæ.

The infection with this strain was transmitted to further series of mice without difficulty. It produced typical febrile reactions in guinea-pigs, and no such reaction in guinea-pigs that had previously been infected with our original strain ("Don."). In the meantime, Derrick had also shown this patient's blood to be specifically infective for the guinea-pig in the manner described in his paper.

This demonstration of Rickettsiæ in mice infected directly with human blood eliminates the possibility that the Rickettsiæ may have been derived from some latent guinea-pig infection.

The Agglutination of Rickettsial Emulsions.

The enormous numbers of Rickettsiæ in certain mouse spleens suggested that it would be possible to obtain suspensions of these for agglutination tests. No difficulty was found in preparing such suspensions from heavily infected spleens. The real difficulty was in obtaining such heavy infections with regularity, and we have not yet found a completely satisfactory method of doing so. It seems necessary (*a*) to use as inoculum an emulsion of heavily infected spleen, (*b*) to inoculate young mice of not more than 20 grammes in weight, and (*c*) to kill them seven or eight days after inoculation. Even when these conditions are all complied with, we find that only about half the spleen smears show really heavy infections with numerous Rickettsiæ in every oil immersion field.

The technique employed is the following:

A number of heavily infected mouse spleens are ground to a smooth paste with sterile quartz powder. The paste is then emulsified in saline solution, about two cubic centimetres per spleen, and centrifuged in an angle centrifuge for five to ten minutes, so that the quartz powder and cells may be deposited. The supernatant fluid is removed to fresh centrifuge tubes and spun in the angle centrifuge for an hour or longer, till the supernatant fluid is almost limpid. The fluid is removed carefully, to avoid dislodging the fine deposit on the side of the tube. The deposit is emulsified in the same amount of saline solution and again centrifuged for one hour. The final deposit is emulsified with a small amount of saline solution and broken up with a pipette. Any clumps are removed by a brief centrifugation, and the emulsion is then diluted to an opacity suitable for agglutination. Smears made from such suspension and stained by Castaneda's method should show Rickettsiæ forming 50% or more of the visible particles. The agglutination is carried out macroscopically according to the usual technique; but owing to the difficulty of obtaining large amounts of suspension, the smallest convenient volumes, 0·05 cubic centimetre each of serum dilution and rickettsial suspension, are used in small agglutination tubes of clear glass. The tubes are placed in a water bath at 45° C. for three hours, and the agglutination is then read. Different suspensions vary somewhat in their susceptibility, and the time required for agglutination may range from one and a half to five hours.

The agglutination is finely granular, except with particularly active sera such as those obtained from experimentally infected monkeys, when relatively large easily visible clumps may be produced. Readings are made with a hand lens, and all doubtful tubes should be compared with the controls, as a slight degree of spontaneous agglutination occurs with some suspensions. Infected livers, some of which contain relatively large numbers of Rickettsiæ, may also serve for the preparation of agglutinating emulsions; but these have proved more unstable than splenic ones in our experience.

Tests with sera from experimentally infected animals have shown that infected monkeys produce a relatively high titre agglutinating serum. Monkeys 3 and 4, inoculated on April 21, 1937, were bled seven, thirteen and twenty-two days later. The results of agglutination tests are given in Table I.

TABLE I.
Agglutination Titres of Monkey Sera.

Time after Inoculation.	Agglutination Titres.	
	Monkey 3.	Monkey 4.
7 days	<2	<2
13 days	2	40
22 days	20	400

Normal monkey serum shows no agglutination. Guinea-pig immune sera usually show agglutination,

[1] Work supported by a grant for research on virus diseases from the Rockefeller Foundation and the Commonwealth Government Department of Health.

[2] Read at the fifth session of the Australasian Medical Congress (British Medical Association), August, 1937.

but not beyond a serum dilution of one part in ten. Since some normal guinea-pig sera show agglutination with undiluted serum, these results are hardly significant.

Tests have now been made on a considerable number of human sera. The results indicate that positive agglutination is diagnostic of "Q" fever, and that, as in the monkeys, agglutinins begin to appear ten to fifteen days after symptoms commence. Figure I shows graphically changes in the agglutination titre of those patients with proved "Q" fever from whom two samples of serum, taken a week or more apart, were available.

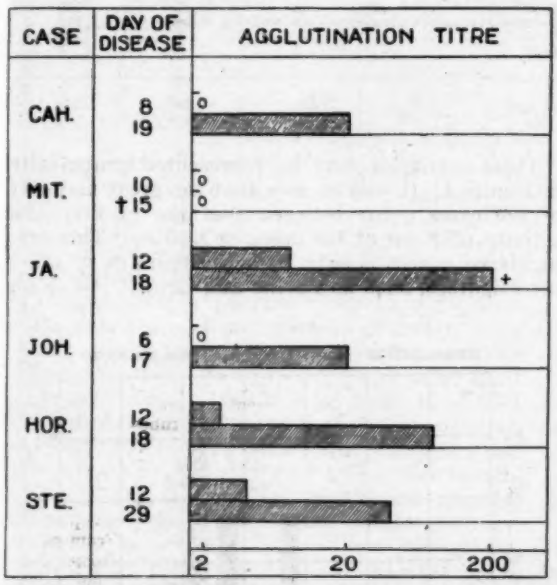

FIGURE I.

Rickettsial agglutination by sera from proved "Q" fever cases.

Table II gives the titres, that is, the highest final dilutions of serum, in which agglutination was clearly visible with a hand lens after four to five hours at 45° C. for all the "Q" fever sera tested. It is of interest that the three sera showing the highest titres were from patients with unusually prolonged periods of fever, "Don.", "Ja." and "Hor." having been febrile for thirty-nine, fifteen and twenty-six days respectively.

Amongst the human sera tested with completely negative results were eight normal adult sera from members of the laboratory staff, serum from a case of proved endemic typhus with a high titre of X.19 agglutination, and sera from several patients with fever of unknown ætiology.

Discussion.

These findings constitute final proof of the rickettsial ætiology of "Q" fever, and provide two diagnostic methods to supplement the guinea-pig test of Derrick. The agglutination test should be of particular value in epidemiological studies. Up to the present we have not been able to undertake any study of how long the rickettsial emulsions remain suitable for agglutination, or of the influence of preservatives. In the refrigerator one preparation remained satisfactory for six weeks without preservative; but detailed studies on these points will be necessary before such emulsions can be issued for routine agglutination tests.

TABLE II.

Agglutination of Rickettsial Emulsion by Patients' Sera.

Patient.	Day of Illness.	Diagnosis of "Q" Fever.	Agglutination Titre.
Don.	37	Proved.	400
Ja.	12	Proved.	8
	18		320
	64		320
Ste.	12	Proved.	4
	29		40
S.T.	17	Proved.	20
	36		20
	66		20
Joh.	6	Proved.	<2
	17		20
Cah.	8	Proved.	<2
	19		20
Hor.	12	Proved.	2 (tr.)
	18		80
Mit.	10	Proved.	<2
	15[1]		<2
Smi.	18	Proved.	8 (weak)
Wen.	15	Probable.	40
Rob.	15	Probable.	2

No further information on the relation of the "Q" fever Rickettsia to the classical forms is available. The absence of agglutination by a serum of known high content in X.19 agglutinins is a further indication that the condition bears no relation to endemic or classical typhus. There are some resemblances between the pathology of psittacosis infection in the mouse and that of "Q" fever, and Lillie (1930) considered that the virus of psittacosis should be regarded as a Rickettsia. For these reasons limited cross-immunity experiments were carried out. Mice immune to "Q" fever were inoculated with an active strain of psittacosis and died with typical *post mortem* findings in the same time as control mice of the same age. We believe that the Rickettsia and the disease it causes are distinct from any previously described; but direct immunological comparison with the various spotted fever (tick-borne) types will be necessary before this can be finally stated.

Summary.

1. Typical "Q" fever Rickettsiæ have been found in the spleens of mice inoculated with blood taken from a patient in the early stage of the disease.

2. Methods of preparing agglutinating suspensions of Rickettsiæ from infected mouse tissues are described.

3. Such suspensions are agglutinated to variable titre by serum taken from patients from ten to fifteen days after the onset of symptoms.

4. The agglutination test is specific for "Q" fever infections.

Brief Clinical Reports of the Cases on which Repeated Agglutination Tests were Performed.

"Don.", Case VII of Derrick's paper, was a braceman on new sewerage excavation work, aged thirty-six years. He had a prolonged, severe illness, associated with jaundice. His temperature returned to normal on about the thirty-ninth day.

"Ja." was a rigger at the abattoirs, aged fifty-seven years. He had a fairly severe infection that lasted for fifteen days. The spleen was palpable. The virus was isolated from both blood and urine.

"Ste." was a meat inspector, aged forty-three years. He had a mild attack, lasting for eight days. The virus was isolated from blood by guinea-pig inoculation on the eighth day.

"S.T." was a meat inspector, aged thirty-five years. He had a short, severe fever lasting for eight to ten days.

"Joh.", a meat inspector, aged thirty years, had a fairly severe attack. His temperature returned to normal on the tenth day, but there was a subsequent relapse.

"Cah." was a tank-house worker at the abattoirs, aged forty-seven years. He had nine days of fever, followed by a mild relapse.

"Hor." was a dairy-farm worker, aged seventeen years, at Gympie. He had a primary fever lasting for nine days, followed by a relapse; his temperature was normal on the twenty-sixth day of his illness.

"Mit.", an abattoir worker, aged sixty-two years, had a fatal infection, complicated by chronic pulmonary tuberculosis. Death occurred on the fifteenth day of his illness.

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PROGNOSIS IN CORONARY OCCLUSION.[1]

By M. D. SILBERBERG, M.D.,

Physician to In-Patients, Alfred Hospital, Melbourne.

THE clinical signs and symptoms of coronary occlusion are now well known. There is little difficulty in diagnosing a typical case; indeed it would be no exaggeration to state that, given an accurate history, it could be diagnosed by correspondence. All cases have not, however, a sharp clinical focus, and many are encountered in which the diagnosis is difficult and doubtful. The case history is all-important in the diagnosis of any type of angina. Insufficient attention to full details of all the circumstances preceding and succeeding the attack leads often to faulty diagnosis. This paper is, however, concerned only with prognosis and is based on an analysis of 335 cases of coronary occlusion observed by me and selected from a total series of 1,335 cases of *angina pectoris*.

The criteria for diagnosis, briefly, consist in a history of an attack of severe and prolonged anginal pain, associated with restlessness, sweating, dyspnœa and some degree of shock and collapse. In 227 cases in the above series electrocardiographic records were obtained. Some degree of abnormality was found to be present in all but two. The abnormality was not, however, necessarily gross or diagnostic of coronary occlusion. In 282 of the 335 cases the outcome is known, either that death occurred or that the patient is still living (Table I).

[1] Read at the fifth session of the Australasian Medical Congress (British Medical Association), August, 1937.

TABLE I.

Distribution of 318 Cases of Coronary Occlusion according to Age and Sex.

Age Period.	Males.	Females.	Total.
20–30	2	2	4
30–40	11	3	14
40–50	47	8	55
50–60	88	17	105
60–70	85	28	113
70–80	17	7	24
80–90	2	1	3
All ages	252	66	318

These statistics may be represented graphically in Figure I. It will be seen that the great majority of the cases occur between the ages of fifty and seventy (218 out of 318 cases, or 68·5%). This case incidence agrees closely with the findings of other investigators, such as Levine and Brown,[1] Connor

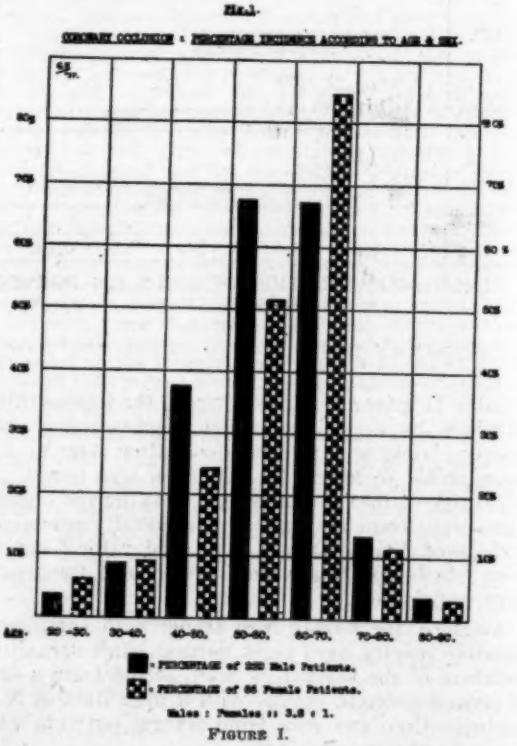

FIGURE I.

and Holt,[2] Parkinson and Bedford[3] and Palmer.[4] It will be further seen that coronary occlusion is approximately four times as common in males as in females, a fact which has been noted by all writers. In the present series, the ratio is

3·8 : 1. This sex incidence has not been satisfactorily explained as yet. Curiously enough, in cases of hyperpiesia females predominate. It is a point of diagnostic importance that angina is very rare in young females, apart from the presence of rheumatic or syphilitic cardio-vascular disease.

Out of 335 patients with coronary occlusion, 133 are known to be dead and 149 living, the remainder being untraced. The duration of life has been calculated from the date of the original coronary occlusion, as deduced from the history, and the findings are set out in Table II.

It should be recognized that group statistics have little bearing on the prognosis of individual cases. The obvious reason for this is that in statistics "average" times are made up of "longs" and "shorts", and such averages are of little value as applied to individuals, seeing that the "longs" may represent years and the "shorts" hours. From a mass of statistics we endeavour to reach generalizations in an attempt to simplify the problem. To most generalizations there are usually many exceptions, and this applies no less to problems of prognosis.

TABLE II.
Duration of Life of 282 Patients who sustained Coronary Occlusion, 133 being now Dead and 149 still Alive

	Time.																																				
	Under 12 Hours.	Days.							Weeks.					Months.												Years.											
		1	2	3	4	5	6	7	1	2	2½	3	4	2	3	4	5	6	7	8	9	10	12	14	15	1½	2	3	3½	4	4½	5	6	7	8	9	10
Died	13	6	8	10	1	1	2	–	3	7	2	2	8	8	6	3	3	4	6	3	1	–	4	1	2	3	9	6	–	5	–	1	2	–	–	3	–
Lived	—	–	–	–	–	–	–	–	–	–	–	–	2	–	5	3	–	2	3	6	1	3	14	1	7	3	23	17	1	16	1	11	15	10	2	2	1

It will be seen from Table II that the time of death ranged from a few hours up to nine years after the original occlusive attack. Further, some of the patients are still living after periods extending from one month to ten years after their initial attack. Among the 133 fatal cases, 13 (9·8%) patients died within twenty-four hours or less. Twenty-eight (21%) died within less than one week. Twenty-two others (16·5%) died within one month, and twenty-four (18%) died within six months. Fourteen more (10·5%) were dead within the year, and another fifteen (11·3%) within two years. Fourteen (10·5%) were dead in less than six years, and three (2·3%) died in the ninth year. These figures may be presented more strikingly in Table III.

TABLE III.
Fate of 133 Patients who eventually Died after Coronary Occlusion, Expressed in Time from the Initial Attack.

Time.	Patients Alive.	Patients Dead.
24 hours	120	13 (9·8%)
1 week	92	41 (30·8%)
1 month	70	63 (47·3%)
6 months	46	87 (65·3%)
1 year	32	101 (75·8%)
2 years	17	116 (87·1%)
6 years	3	130 (97·7%)
9 years	0	133 (100·0%)

Of 149 patients known to be still living, some were examined quite recently and some in previous years, but no cases are included since May 31, 1937. Thirty-nine patients (26·2%) have survived for one year. Thirty-four (22·8%) have lived for between one and two years. Forty-six patients (30·8%) have survived for periods up to five years, and twenty-five (16·9%) up to seven years. Five patients (3·4%) have lived for a period of between eight and ten years.

Electrocardiograms and Prognosis of Coronary Occlusion.

Electrocardiograms represent electrical changes resulting from the excitation-contraction processes in the heart muscle. If pathological lesions occur, the cardiograms show departures from the normal form of the complexes, particularly in regard to the *RT* and *T* waves. Hence significant changes are valuable corroborative evidence of myocardial lesions such as result from coronary occlusion. In the mass, significant *RT* and *T* variations carry a baneful prognosis, but in my experience one should not draw dogmatic, far-reaching conclusions from such abnormal curves when applied to individual cases. Thus in Figures II to X examples are shown of significant variations not associated with early death. Nevertheless normal or nearly normal electrocardiograms are associated with better prognosis than are abnormal curves.

If following an attack of coronary occlusion a series of curves shows progressive approach to normality, then this is evidence of reparative processes in the muscle area affected, and therefore of improved prognosis. The changes in the electrocardiographic complexes vary according to the time which has elapsed since the coronary occlusion; hence significant *RT* and *T* variations are not necessarily comparable unless the time intervals from the attack correspond. For this reason single cardiographic examinations are not so informative as is a series of observations over a period of weeks or months (*vide* Figures II to X). Electrocardiograms are not a guide as to the imminence of death. In a large series of curves illustrating some particular type of *RT* or *T* abnormality, the average prognosis will be serious, but, as mentioned above in reference to "averaged" statistics, the application to an individual case is not at all reliable.

Pathology of Coronary Occlusion.

Coronary occlusion occurs as the result of the effects of arteriosclerosis and of atheroma. Many pathologists group these processes together under the term "atherosclerosis". It is unfortunate that the essential facts in the ætiology of either condition are as yet unsettled, nor is it by any means established that the fundamental causations are related. There is no disagreement, however, that

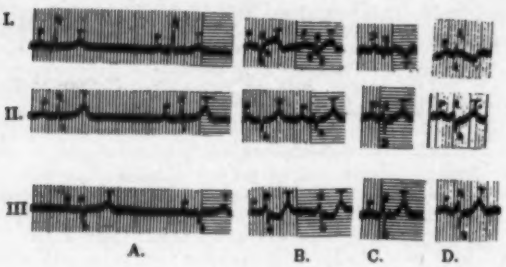

FIGURE II.

Case I: Male (R) aged 51 years. A: Bradycardia, 38 per minute. B: Elevated, domed *RT* I, depressed *RT* III. C: *RT* I less domed, *T* I inverted, *RT* III not depressed, *T* III tall, *T* I less inverted. Living and well (1937).

these pathological processes are frequently found together in the latter period of life. The occlusive process most commonly affects the left anterior descending branch, but any part of the coronary

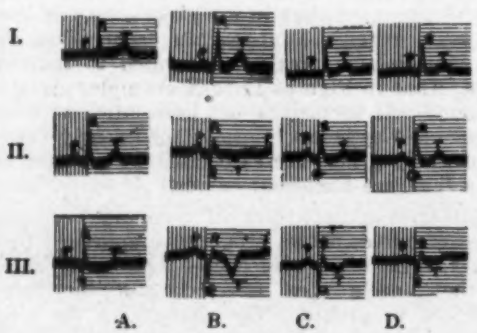

FIGURE III.

Case II: Male (F.S.) aged 47 years. A: In attack. *RT* III depressed. B: *T* II slightly inverted, *Q* III well marked, *T* III deep inversion. C: *T* II upright, *T* III diminished negativity. D: *Q* III diminished, *T* III negativity diminished. Living and well (1937).

arterial system may be involved, either extensively or locally, and in either large or small branches. The occlusive changes produced by thickening of the intima, by fibrosis of the middle coat or by atheromatous plaques may lead to various ischæmic lesions in the myocardium in which coronary thrombosis may or may not play a part. Sudden deprivation of blood supply may cause infarction, which may lead to softening of a local area of the heart wall, subsequent aneurysmal bulging and even rupture. Extension of the infarction process to the endocardial surface is frequently followed by the formation of mural thrombus, a common source of emboli in such cases. Gradual ischæmia, on the other hand,

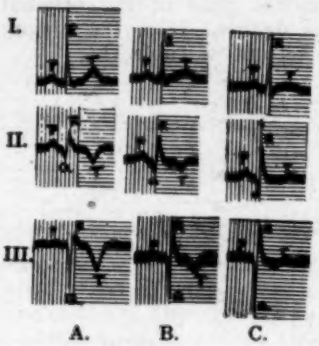

FIGURE IV.

Case III: Male (W.R.) aged 39 years. A: *T* II negative, *Q* III very marked, *T* III deeply negative. B: *T* II, *T* III diminished negativity. C: *T* I flattened, *T* II, *T* III almost flat, *Q* III (11 m.m.). Living and well (1937).

may lead to atrophy and thinning of the ventricular wall, which may become merely fibrous, practically no muscle remaining.

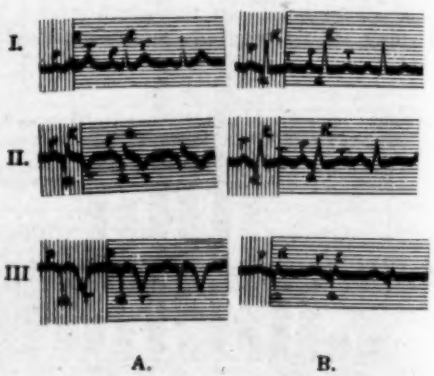

FIGURE V.

Case IV: Male (E.C.). A: *Q* II, *Q* III well marked, *T* II, *T* III deeply negative. B: *Q* II normal, *Q* III slight, *T* II upright, *T* III flat. Living (1937).

The use of the term "coronary thrombosis" has become universally current, but modern pathologists stress the fact that definite thrombosis is relatively

rare. For this reason the term "coronary occlusion" is preferred in the present paper, because the occlusive process is greatly predominant at autopsy. Dr. R. J. Wright-Smith,[5] Government pathologist in Victoria and pathologist to the Royal Melbourne Hospital, analysed 1,371 *post mortem* examinations ordered by the coroner, and 3,800 similar examinations at the Royal Melbourne Hospital. Many of the coroner's cases came to autopsy because of sudden

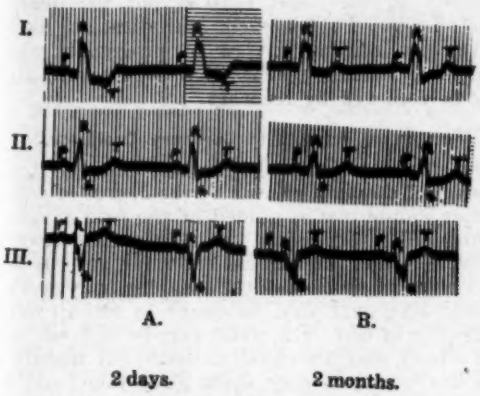

FIGURE VI.
Case V: Male (C.D.) aged 57 years (June 4, 1935). A and B: Bundle branch lesions. Well and working hard (1937).

death. Of the 1,371 *post mortem* examinations, 24% showed coronary obstruction. Out of 339 such cases, 92·9% showed atheromatous occlusion and only 7% thrombosis. In the hospital series of 3,800 cases,

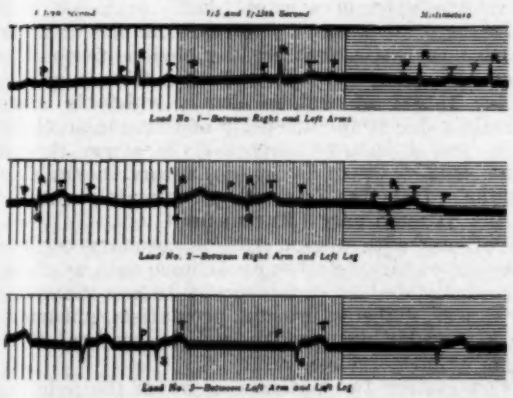

FIGURE VIIA.
Case VI: Male (W.G.) aged 67 years (August 28, 1936). Thirty hours after attack 2:1 heart block.

4% showed extensive coronary lesions; out of 156 such cases 86·6% were due to atherosclerosis and only 13·4% proved to be coronary thrombosis. Dr. Rupert Willis, pathologist to the Alfred Hospital, Melbourne, in a personal communication, states that since August 4, 1935, 622 *post mortem* examinations were performed in the hospital. Forty-one cases (6·6%), twenty-six male and fifteen female subjects, showed pronounced coronary lesions, such as atheroma or calcification. In only seven were gross complications present; five of these were cases of cardiac aneurysm, one presented rupture of a coronary artery, and only one was a case of coronary thrombosis. It appears, therefore, that clinicians use the term "coronary thrombosis" much too freely, and that "coronary occlusion" should be preferred as a better and a more comprehensive

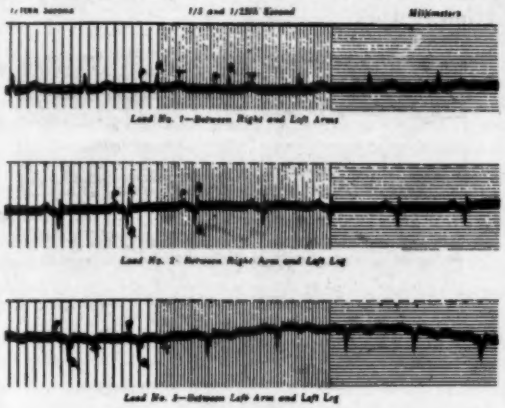

FIGURE VIIB.
Case VI: Male (W.G.) aged 67 years. Six months later no heart block, *Q* II, *Q* III well marked, *T* III slightly negative.

term, because it includes all forms of coronary obstruction.

Gross pathological changes in coronary arteries may exist without any history of angina, so that Parkinson and Bedford[6] are too dogmatic in

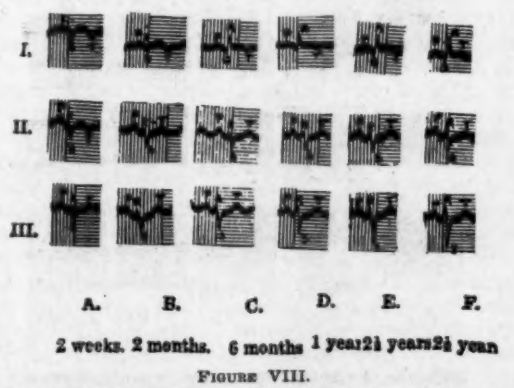

FIGURE VIII.
Case VII: Male (V.M.) aged 36 years. A: *ST* I domed, *T* I negative, *T* II negative. Low voltage curves. B: *T* II upright. C: *R* I increased, *T* negativity diminished. D: Unchanged. E: Unchanged. F: Unchanged. Patient well (1937).

stating that "the problem of angina has been nailed forever to the tree of decaying coronary arteries". Patients with gross coronary lesions may die from such other causes as malignant disease, cerebral apoplexy, uræmia *et cetera* without manifesting angina.

One is often amazed at autopsy on elderly subjects presenting advanced coronary atherosclerosis, not by the fact of death, but by the patient's having managed to live so long with such extensive pathological changes in the coronary circulation. The reason is probably to be found in the fact that extensive anastomoses occur in the precapillary branches, aided, according to some authorities, by the Thebesian circulation. It is this factor of anastomosis which is the basis of recovery as seen in clinical work.

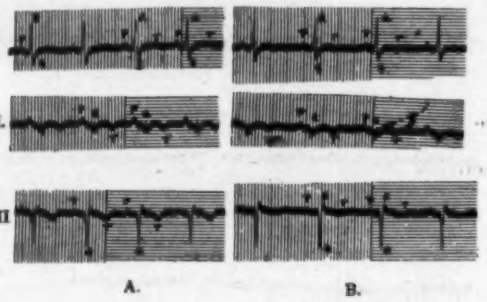

FIGURE IX.

Case VIII: Male (F.L.) aged 43 years (August 11, 1934). A: *T* I flat, *RT* II domed, and *T* II negative. (Pardee wave), *Q* III marked, *T* III negative. B: *T* I slightly negative, *RT* II and *T* II doming and negativity diminished, *T* III negativity diminished. Patient living and well (1937).

Richard C. Cabot, in "Facts of the Heart" (1926),[6] quotes 94 *post mortem* cases with pronounced coronary sclerotic changes without a history of angina.

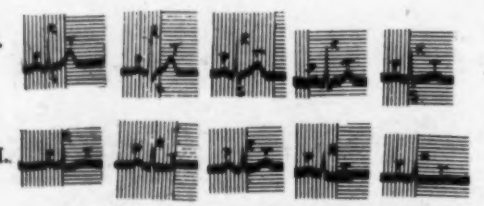

FIGURE X.

Case IX: Male (H.R.) aged 39 years. A: *T* III deeply negative. B: *T* II slightly diphasic, *T* III deeply negative. D similar to C: *T* II slightly diphasic. E: *T* III diminished negativity, Lead IV (not shown) normal. Patient has mild angina of effort.

This is illustrated by the case of a recent out-patient of the Alfred Hospital, who for five years was under treatment for pernicious anæmia and responded well to the usual liver therapy. During this time he made no complaint of anginal pain. He was then admitted as an in-patient with rapid heart failure and died within forty-eight hours. Autopsy revealed extensive atheromatous changes throughout the entire coronary system, including the orifices of the vessels, without evidence of coronary thrombosis or infarction.

If we view prognosis from a pathological standpoint, there can be little reason to doubt that the severity of the attack will depend on the rapidity of the final occlusive process and on the size of the branch involved, as well as on the preceding integrity of the heart muscle and the degree of anastomosis. *Post mortem* statistics are likely to convey too serious a view of prognosis, whereas clinical experience teaches that even severe attacks may be followed by recovery.

Clinical Aspects of Coronary Occlusion.

One cannot judge prognosis entirely by the severity of the pain or even by the degree of collapse. Rather should one be guided by the rate of recovery or downhill progression. Thus, a patient may have a severe attack of anginal pain for several hours, with signs of shock and collapse, but may feel quite comfortable next day, be eager to sit up or even to get out of bed. His pulse may be of good volume and steady and his blood pressure not unduly low. His heart sounds may show good tone, and there may be no basal crepitations in his lungs. Such a patient may be deemed to have suffered only a small occlusion and to have a good prognosis. At the same time, there is no guarantee that recurrence will not take place, possibly with crippling effects or even a fatal result on the next occasion. In any case, it is wise to play for safety by keeping such a patient at rest, in order to allow the myocardial changes to improve as tissue reaction subsides and anastomosis becomes established.

In the present series of cases, examples of sudden death in a first attack are, for obvious reasons, not included. Any patient suffering from angina is under threat of sudden death, which is almost certainly due to the inception of ventricular fibrillation, yet it is most important to stress the fact that sudden death is by no means inevitable in angina. It is the fate of approximately one-third of the patients only (Mackenzie[7]).

Patients with angina and/or coronary occlusion may die of various other conditions, such as chronic myocardial failure, intercurrent disease exemplified by cancer, diabetes, uræmia, prostatism, pneumonia, or a vascular catastrophe such as cerebral thrombosis or hæmorrhage.

Contrasting two patients in whom the pain is of equal severity, one having old-standing cardiovascular disease and one without such, the prognosis will usually be more serious in the former type of patient. The presence of an enlarged heart, thickened arteries or chronic valvular disease usually indicates a graver prognosis than when these signs are absent. This rule cannot be absolute, because a well-defined plaque of atheroma in a large coronary branch may present no clinical signs, yet may be the cause of extensive occlusion. It can also be stated that, in two cases of equal severity, one with normal and one with abnormal electro-

cardiograms, more serious prognosis will appertain to the latter.

Patchy atheroma of the coronary arteries is of frequent occurrence in the aged and is relatively common even in groups of younger patients, as was demonstrated by *post mortem* examinations of German soldiers in the Great War.[8] Between the ages of twenty and thirty, 10% of these men, physically selected though they were, showed definite coronary sclerosis.

Another obvious generalization is that a multiplicity of serious signs following an attack of occlusion means a graver prognosis. Thus the presence of feeble heart sounds, gallop rhythm, low blood pressure, *pulsus alternans*, basal crepitations and cyanosis obviously indicates such a state of affairs that it is merely a matter of degree till the evidence of impending death is unmistakable.

The degree of collapse is important and a good guide to prognosis. The immediate gravity is in many cases only too obvious. When the patient is almost moribund he presents a combination of the signs of central and peripheral circulatory failure. The heart sounds are feeble and usually increased in rate; gallop rhythm may be present, with or without extra systoles. Vaquez[9] has drawn attention to a triad of signs of serious prognostic significance, which he takes to denote failure of the left ventricle, and which comprise tachycardia, gallop rhythm and extra systoles.

In coronary occlusion, the blood pressure is usually strikingly low and the radial pulse may be impalpable. Peripheral failure is indicated especially by a leaden, cyanotic hue in the finger nails and by sluggish capillary circulation with low blood pressure. The mental alertness of some patients who are obviously rapidly dying is extraordinary in view of their extremely inadequate circulation. Despite the extreme physical and circulatory enfeeblement, the patient may yet be able to give a clear account of the details of the attack or be fully aware of his impending dissolution. It is strikingly impressive to find a patient livid, pulseless and dying, yet anxious to give active cooperation in the examination. On the other hand, some patients who appear to be desperately ill may yet make a satisfactory recovery. Speaking generally, there is about a 50% chance of recovery from a first attack.

The severity of symptoms alone is not a safe guide to prognosis. In particular, the degree of pain may be misleading. Tolerance for pain is largely a matter of temperament. The threshold for pain from the same degree of stimulus varies in different individuals. It is a most difficult practical problem to evaluate the severity of subjective phenomena, and to do so requires considerable experience and a sound knowledge of human nature. It is just as easy to over-estimate as to under-estimate the severity of pain, unless due allowance is made for the phlegmatic or hypersensitive temperament. Similarly, the degree of anxiety and shock must be likewise assessed.

The presence of a pericardial rub does not, *ipso facto*, mean a serious prognosis. It indicates involvement of an anterior branch rather than a posterior branch, but such location may be no more significant.

The age of the patient is a relative standard only. Obviously, at the extreme of old age any serious event is a grave handicap. On the other hand, the latter period of life is often accompanied by better coronary anastomosis in the pre-capillary vessels than is found in younger patients (Gross[10]). This probably explains the remarkable recovery demonstrated by some elderly patients.

Recurrence of attacks is an obvious calamity and must necessarily lessen the expectancy of life, yet some patients do attain satisfactory efficiency even in the face of such odds. It is not uncommon for the pathologist to examine hearts showing multiple scars, the readiest explanation for which is coronary occlusion in small branches, but such lesions are not necessarily related to the cause of death.

The occurrence of angina of effort after coronary occlusion is not unusual, but the prognosis cannot be directly correlated. It is a curious phenomenon that, on the other hand, angina of effort ceases in a percentage of cases. The explanation is not easy: apparently it is unrelated to fall in blood pressure. Lewis[11] suggests that the absence of pain may be due to a killing off by ischæmia of the muscle area and the nerve terminals involved. It might be argued, however, that establishment of an efficient anastomosis is the more likely explanation. The question is still unsettled.

Previous habits, such as chronic alcoholism, count much in the prognosis. Similarly, preexisting diseases will be associated with a worse prognosis than will the possession of a clear past history.

The prognosis is adversely affected by the presence of such common conditions as recurrent bronchitis, emphysema, asthma, arteriosclerosis, diabetes, gout, chronic nephritis, chronic valvular disease, gall-bladder disease, cirrhosis of the liver, obesity, prostatism and recent influenza.

Occupation has no direct bearing on prognosis, except as regards recovery of physical efficiency for heavy work. After coronary occlusion the capacity for exertion is often surprisingly good, and some patients can even play golf without symptoms and undertake a fair degree of manual exertion.

Complications, such as pulmonary embolism, may seriously affect the immediate outlook, occasionally being fatal or leading to pleurisy or consolidation of the lung. Cerebral or peripheral emboli may occur; sometimes gangrene of a limb may result from the latter. Such catastrophes as cardiac aneurysm are obviously dangerous and rupture of the heart is necessarily fatal.

Syncope, associated with anginal pain, may be synonymous with the occurrence of coronary occlusion. At the time of the attack the patient appears to be moribund, and even in the immediate period of recovery will appear to be desperately ill because of the pallor, dilated pupils, slow pulse, low blood pressure, sighing respirations, sweating and

faint heart sounds. Recovery may yet be completely satisfactory. These syncopal seizures create difficulty in diagnosis, and, unless the association of pain is elicited, the occurrence of coronary occlusion may be readily overlooked.

A sharp fall of blood pressure below the normal reading for that particular patient is to be expected after the onset of an attack, and is not a reliable prognostic guide. In contrast, a rapidly and progressively falling blood pressure may be very significant. Particularly is this so in the presence of low pulse pressure. The pulse may completely disappear at the radial artery and be palpable only at the brachial; naturally, in such circumstances patients rarely recover. The blood pressure may here scarcely register, especially the diastolic. A sign of similar import is the presence of a soft eyeball.

It is a favourable sign if the patient soon feels more comfortable and is more cheerful, if his colour improves and his pulse rate becomes slower and of fuller volume, with rising blood pressure (although this latter may not appear for some days). It is also favourable if the heart sounds improve in tone. On the contrary, cardiac enlargement and persistence of gallop rhythm, with or without *pulsus alternans*, indicate that the myocardium has been seriously damaged. In such circumstances patients recover, if at all, with only a limited degree of cardiac reserve. In about three months after the development of such signs further dilatation frequently occurs and then congestive failure usually sets in.

The appearance of marked arrhythmia, such as paroxysmal tachycardia or auricular fibrillation, may be serious but is not necessarily so, particularly if the irregularity responds readily to treatment. Quinidine sulphate may arrest the arrhythmia, and this drug is the best treatment for ventricular paroxysms.

The management of cases is often the determining factor in the prognosis. There is a type of case in which the degree of angina is of gradually increasing intensity. It may commence as the angina of effort, but gradually the pain begins to appear even while the patient is at rest. These crescendo cases are most probably due to a gradual occlusive process in a coronary branch. It is most important to recognize them. Too often it happens that they are not comprehended and the patient is allowed to continue his usual routine until a very severe and prolonged attack occurs, when the prognosis is so much the worse. If these cases are recognized the patient should be put to bed for at least a month. This gives opportunity for collateral circulation to be established and for the heart to adjust itself. Unfortunately there is no guarantee that such a favourable course will follow rest in bed, yet to ignore the potentialities of danger in this group is to court disaster. It is this class of patient which justifies the treatment of angina by prolonged rest, this being unnecessary in the ordinary case.

Speaking generally, every grade of recovery is possible after an attack of coronary occlusion. It may be a very minor grade, leaving the patient more or less invalided owing to myocardial weakness. In higher grades of recovery, light exertion is possible. In a favourable minority, complete recovery occurs, so that the patient may resume free activity and do a reasonable amount of manual work. When recovery is rapid, we may from a clinical viewpoint usefully visualize these cases as occlusions of a small branch of a coronary artery, with a favourable prognosis.

Summary and Conclusions.

1. Three hundred and thirty-five cases of coronary occlusion have been analysed. The ratio of males to females was 3·8 :1.

2. The ages were recorded in 318 cases; the majority (65·4%) of cases occurred between the fifth and seventh decades. The youngest patient was a male aged twenty-three years; the oldest, a male aged eighty-six years.

3. One hundred and thirty-three patients are known to be dead and one hundred and forty-nine are still living. Fifty-three are untraced.

4. Death occurred within twenty-four hours in thirteen cases, or 9·8%. Three patients survived until the ninth year; five are still living after a period of between eight and ten years since the initial attack.

5. Averaged statistics are of little value when applied to individual cases.

6. Electrocardiograms are more useful in diagnosis than in prognosis, except when a series of curves is obtained over a period of several months.

7. Coronary thrombosis is not usually found at autopsy; hence the term "coronary occlusion" is to be preferred in clinical diagnosis.

8. An attempt should always be made to visualize (*a*) whether actual infarction has occurred, judged partly by the severity of the attack and partly by a rise in temperature for several days, (*b*) whether a small or a large branch of a coronary artery is involved, as estimated mainly by the rapidity of recovery from the initial symptoms of pain and collapse.

9. The prognosis is usually worse in the presence of pronounced signs of cardiac enlargement and arteriosclerosis, but fatal cases are not uncommon when physical signs are slight or absent. Coronary atheroma may exist without apparent clinical signs or symptoms.

10. The presence of signs indicating central and peripheral circulatory failure is of grave prognostic significance.

11. Single symptoms, such as pain, or single signs, such as low blood pressure or the presence of pericardial friction, are not reliable guides to prognosis.

12. Prognosis is seriously affected by the presence of other general or systemic diseases such as bronchitis or renal degeneration.

13. The importance is stressed of recognizing the "crescendo" type of coronary occlusion, that is, when the advancing coronary occlusion results in the production of anginal symptoms from progressively less and less effort.

14. Excellent recovery may occur in cases of coronary occlusion, even in those of great severity.

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SOME LABORATORY EXPERIMENTS WITH A SYDNEY STRAIN OF POLIOMYELITIS VIRUS.

By W. C. SAWERS, D.S.O., M.B., D.P.H., D.T.M.

(From the School of Public Health and Tropical Medicine, University of Sydney.)

THE present epidemic of poliomyelitis in Melbourne and the possibility of a recrudescence of cases in New South Wales have drawn attention to the difficult problems associated with this disease; and it is thus perhaps opportune to record briefly the main features of some animal experiments carried out during and after the 1931-1932 epidemic in New South Wales.

In December, 1931, the Infantile Paralysis Committee of New South Wales drew attention to the possibility of a shortage of serum owing to the scarcity of available donors of blood in New South Wales, and suggested the testing of the serum of adults, or adults who had had the disease in childhood, and of its use if it was found effective. To do this, and to undertake additional investigations when possible, a research subcommittee was formed with Dr. A. H. Tebbutt as honorary director, and by arrangement with the Director-General of Health and the Director of the School of Public Health and Tropical Medicine the laboratory work was carried out at this school.

Animals for Experiments.

Experimental work in poliomyelitis is difficult, in that the only suitable animal is the monkey, and this animal is relatively expensive and difficult to handle. In general, transmission of the disease to other laboratory or domestic animals has not been achieved, though there has been some difference of opinion in regard to the susceptibility of the rabbit.(1) Supplies of monkeys (*Macacus rhesus*) were obtained from Calcutta through the Taronga Zoological Park Trust, and were the principal animals utilized. The monkeys received were healthy, with the following exceptions: some of the first batch proved to be infected with tuberculosis, and it was noticeable that these animals could be detected, as they were viciously attacked by the healthy monkeys; in a later consignment dysentery bacilli (Flexner type) were isolated from one monkey.

Virus.

As the testing of convalescent sera was a matter of urgency, work was commenced with a Melbourne strain of virus that was kindly supplied by Dr. F. M. Burnet, of the Walter and Eliza Hall Institute.

Neutralization tests were carried out by the usual technique of mixing various dilutions of the sera to be tested with an estimated paralytic dose of the virus, the mixture being left overnight in the refrigerator and inoculated intracerebrally into monkeys. The control animals were inoculated with virus *plus* saline solution.

A number of sera were tested, but the results, although suggestive, were indecisive, as on two occasions control animals failed to show paralysis. That this was not due to insusceptibility was shown by the later infection of one of these animals by a Sydney virus.

Sydney Virus.

Owing to these inconstant results, and also to the advisability of obtaining a Sydney strain of poliomyelitis virus, an attempt was made to infect a monkey from a child who had died from the disease. The cord was obtained of a girl, aged seven years, who became ill on January 16, 1932, and died on January 20, 1932, the diagnosis being acute poliomyelitis. On February 22, a 10% suspension of the dorsal area of the cord was prepared, and after a sterility test for other organisms had given no results, approximately 0·5 cubic centimetre was inoculated intracerebrally and two cubic centimetres were inoculated intraperitoneally into a large *Macacus rhesus* monkey weighing 6·8 kilograms (15 pounds). Paralysis occurred in seven days and the animal was chloroformed on the eighth day; the cord was removed, cut into sections and preserved in 50% glycerine saline solution.

Properties of the Sydney Virus.—During the first six passages some fluctuations in virulence were noticeable, in that although 0·5 cubic centimetre of infected cord produced paralysis in all inoculated animals, the onset of paralysis varied from six to twenty-one days. Subsequently, with intracerebral doses of 0·5 cubic centimetre of 10% cord suspension *plus* 0·5 cubic centimetre of saline solution, 17 out of 18 monkeys inoculated for control purposes became paralysed; the longest incubation period was twelve days, and the shortest was four days, an average of approximately 7·4 days. One monkey failed to contract paralysis, but the virus used came from an animal that was chloroformed as late as six days after the onset of paralysis. As this monkey when reinoculated from another cord became paralysed, it is probable that the delay was responsible for the

loss of virulence. In a titration test the smallest dose that produced paralysis was 0·01 cubic centimetre of a 10% suspension of mixed cord. Nasal infections were obtained by the instillation of virus and saline solution.

Preservation of the Sydney Virus.—This strain of Sydney virus was isolated in March, 1932, and when tested in December, 1936, was still potent. The cord used in the last inoculation had been kept in the refrigerator in 50% glycerine saline solution for two and a half years.

Effect on Monkeys.—Infection in these monkeys could be detected in the great majority of cases by signs of excitement and irritability one to two days before paralysis; and a rise in the rectal temperature occurred before the onset of paralysis.

Effect on Other Animals.—To distinguish this Sydney virus from "X" disease virus[2] various animals were inoculated. The results are shown in Table I.

Later, a mixed suspension from the cords of the sheep and the calf was inoculated intracerebrally into a monkey. No paralysis resulted. Thus no evidence was obtained that the Sydney virus infected these animals.

Neutralization Tests.

Neutralization tests were undertaken for the evaluation of the potency of "donor" and other sera. The details of the most extensive test are recorded as illustrating some points of interest. The sera tested were: (i) pooled convalescent sera from Sydney; (ii) pooled convalescent sera from Adelaide; (iii) serum from a normal infant aged two years, and as far as was known unexposed to infection; (iv) serum from a sheep inoculated with virus. This serum (iv) was received per courtesy of Miss B. F. Howitt, of the University of California, United States of America, with the following data:

Sheep 117 was immunized to poliomyelitis monkey virus over a three-year period. The serum sent has not yet been tested, but that obtained at the trial bleeding on September 9, 1931, proved quite potent. When tested for neutralizing ability *in vitro* according to the method of Fairbrother, the following results were obtained.

Monkey 764: 0·6 c.c. serum + 0·4 c.c. 5% virus neutralized.
Monkey 765: 0·4 c.c. serum + 0·4 c.c. 5% virus neutralized.
+ 0·2 c.c. NaCl neutralized.
Monkey 766: 0·4 c.c. serum + 0·6 c.c. virus neutralized.
Monkey 768: 0·2 c.c. serum + 0·6 c.c. virus neutralized.
+ 0·2 c.c. NaCl neutralized.

The controls with normal sheep serum developed the disease when the same dilutions were used.

Virus.

The virus used was a 10% suspension of the cord of Sydney monkey 37, the seventh monkey passage from the original human cord. In a preliminary test 0·5 cubic centimetre of virus *plus* 0·5 cubic centimetre of saline solution produced paralysis in six days. The mode of inoculation was intracerebral. The mixtures of serum and virus were prepared, shaken well, and placed in the incubator at 37° C. for two hours, and then overnight they were placed in the refrigerator. The total dose in each case was made up to one cubic centimetre with sterile saline solution. All sixteen monkeys were inoculated on the same day. The results are given in Table II.

Normal Sheep Serum.

Somewhat later the effect of normal sheep serum was tested; 0·05 cubic centimetre of virus *plus* 0·95 cubic centimetre of normal sheep serum were inoculated intracerebrally into a monkey. Paralysis resulted in six days.

It is noted that the American sheep serum neutralized the virus in all animals, that double the amount of normal infant serum failed to neutralize the virus, and that the two batches of pooled donor sera gave partial neutralization in a similar dosage to the American sheep serum, but not to the same extent. These results strongly suggest that the American strain of poliomyelitis virus and the strain isolated in Sydney are similar. This indication is somewhat contrary to the conclusion of Burnet and Macnamara,[3] who considered that a

TABLE I.

Animal Inoculated.	Intracerebral Dose of 10% Cord Suspension in Cubic Centimetres.	Remarks.	Control Animal Inoculated.	Intracerebral Dose of 10% Cord Suspension in Cubic Centimetres.	Remarks.
Sheep 1	2	Killed 41 days later.	Monkey A.	0·5	Signs of paralysis appeared in six days.
Sheep 2	2	No signs suggesting infection were observed during life or *post mortem* macroscopically or microscopically.	Monkey B.	0·25	Signs of paralysis appeared in eleven days.
Calf	3				
			Monkey C.	0·5	Signs of paralysis appeared in eight days.
Rabbit 1	0·5	No signs suggesting infection were detected.	Monkey D.	0·5	Signs of paralysis appeared in eleven days.
Rabbit 2	0·5		Monkey E.	0·5	Signs of paralysis appeared in six days.

TABLE II.

Sydney Convalescent Serum, Batch 25.		Adelaide Convalescent Serum.		Normal Infant Serum.		American Sheep Serum.		Controls.		
Dose in Cubic Centimetres.[1]	Remarks.	Dose in Cubic Centimetres.	Remarks.	Dose in Cubic Centimetres.	Remarks.	Dose in Cubic Centimetres.	Remarks.	Number.	Dose of Virus in Cubic Centimetres.	Remarks.
0·2	No paralysis.	0·2	Paralysis in 12 days.	0·5	Paralysis in 8 days.	0·2	No paralysis.	1	0·5	Paralysis in 7 days.
0·1	No paralysis.	0·1	No paralysis.	0·25	Paralysis in 6 days.	0·1	No paralysis.	2	0·25	Paralysis in 10 days.
								3	0·1	Paralysis in 8 days.
0·05	Paralysis in 25 days.	0·05	Paralysis in 10 days.	0·1	Paralysis in 10 days.	0·05	No paralysis.	4	0·05	Paralysis in 8 days.

[1] The dose represents the amount of serum; in each instance 0·5 cubic centimetre of virus was added.

poliomyelitic virus derived from a child who died in Melbourne showed distinct immunological differences from the Rockefeller Institute "mixed virus".

Prophylactic Test.

As American sheep serum had proved to be the most efficient in neutralization tests, it was tested to discover whether intravenous inoculation would be effective in protecting monkeys against the virus of poliomyelitis.

The following results were obtained:

Monkey 70 received five cubic centimetres of American sheep serum intravenously, followed immediately by 0·5 cubic centimetre of Sydney virus *plus* 0·5 cubic centimetre of saline solution intracerebrally. Paralysis occurred in five days; Monkey 71 was treated in the same manner, and paralysis occurred in six days; Monkey 72 was treated in the same manner, and paralysis occurred in six days.

Thus five cubic centimetres of immune sheep serum failed to protect monkeys, though it was given at the same time as the intracerebral inoculation of 0·5 cubic centimetre of virus. As the average weight of these three monkeys was approximately 2·5 kilograms (five and a half pounds), the five cubic centimetres of serum in the case of the monkeys would be equivalent to 40 to 50 cubic centimetres of serum to a child weighing 22·6 kilograms (fifty pounds). Therefore no evidence was obtained in this experiment to indicate beneficial results from serum used therapeutically. It is, of course, recognized that the method of infection used was a severe one and that other factors also were not comparable with human infections.

Summary.

1. The isolation of a Sydney strain of poliomyelitis virus has been recorded.

2. The effect of this virus on monkeys and other animals has been studied.

3. The virus has been used in neutralization tests and in protective tests. Of special interest was the high neutralization effect of immunized sheep serum from the United States of America when tested against the Sydney strain of virus; this pointed to a similarity of virus strains.

This work was carried out in cooperation with the Infantile Paralysis Committee of New South Wales and with the assistance of Dr. A. H. Tebbutt, honorary director of the paralysis committee, and of Dr. Karen Helms, medical officer and secretary.

Acknowledgements.

Grateful acknowledgement is made to the Taronga Park Trust for help in the supply of monkeys; to the Director of Veterinary Research for facilities in sheep and calf experiments; to the members of the Tropical School; and in particular to Mr. F. R. Barrett and to Mr. J. W. Fielding, who assisted throughout this work, and to all others who gave advice and help.

References.

(1) Report of the Poliomyelitis International Committee for the Study of Infantile Paralysis, page 101.
(2) J. B. Cleland, A. W. Campbell and B. Bradley: "The Australian Epidemics of an Acute Polio-Encephalo-Myelitis (X Disease)", Eighth Report of the Microbiological Laboratory, New South Wales, for the year 1917.
(3) F. M. Burnet and J. Macnamara: "Immunological Differences between Strains of Poliomyelitic Virus", *The British Journal of Experimental Pathology*, Volume XII, 1931, page 61.

Reviews.

PROGRESS IN ANÆSTHESIA AND ANALGESIA.

PROGRESS in anæsthesia has been so rapid during the last five years as to require a second edition of Dr. Langton Hewer's "Recent Advances in Anæsthesia and Analgesia". This excellent little book has been virtually rewritten, and, in spite of the employment of smaller type, the inclusion of fresh material has necessitated the addition of a further eighty-five pages.[1]

Amongst the new agents described are cyclopropane, di-vinyl ether, "Evipan sodium" and "Pentothal sodium". The more established drugs and methods are reviewed in the light of recent researches and a very full bibliography is placed at the end of each chapter so that the reader may follow with ease any subject of special interest. Although the general arrangement of the book is unchanged, two new chapters are added which are devoted to oxygen and carbon dioxide therapy respectively. This follows the American

[1] "Recent Advances in Anæsthesia and Analgesia (Including Oxygen Therapy)", by C. L. Hewer, M.B., B.S.; Second Edition; 1937. London: J. and A. Churchill Limited. Demy 8vo, pp. 292, with 113 illustrations. Price: 15s. net.

plan where the department of oxygen therapy is usually a subdivision of that of anæsthesia.

The opening chapter on theoretical considerations and their practical application is excellent; it is a concise review showing mature judgement and plain common sense. The chapter on premedication deals with the numerous methods and shows their relative advantages and disadvantages. Stress is laid on the dangers of excessive premedication, which has been shown to increase the incidence of post-operative pulmonary complications.

Collapse and resuscitation during anæstheisa are discussed fully and a definite plan of action is outlined. There is an illustration of the author's own cardiac puncture needle, which is designed for auricular puncture. It has been shown that the auricles are more sensitive to stimulus than the ventricles.

Recent developments in endotracheal anæsthesia are considered adequately and concisely; but there are still many who will disagree that "the true insufflation technique is now obsolete". The present position of spinal analgesia is reviewed and "Percaine", used by the Howard Jones technique, is considered to be the agent of choice for abdominal work. It is suggested that low spinal block is destined to replace extradural and transsacral block for perineal operations, as the results appear to be more certain and the technique is easier and safer. "Stovaine" is advised for this purpose, but no mention is made of "heavy 'Percaine'" which produces analgesia that is equally good and of much longer duration. Much sound advice is contained in the chapters devoted to anæsthesia for thyreoid, thoracic and abdominal surgery. Dr. Hewer has a large experience of thyreoid operations and gives the details of his methods. For toxic goitres he uses "Avertin" as a basal narcotic, a hypodermic injection of scopolamine and a small dose of morphine are given, these are followed by nitrous oxide and oxygen, and the neck is infiltrated with local anæsthetic. Cyclopropane is considered to be the anæsthetic of choice for total thyreoidectomy in the treatment of congestive heart failure.

In intestinal obstruction the use of endotracheal methods is advised. Unfortunately the adoption of this sound advice is not always possible as the patient is apt to vomit before anæsthesia is sufficiently deep for intubation and suffocation by inhalation of vomitus may occur. There is no mention of pre-operative treatment by Wangensteen's method of gastro-duodenal suction siphonage combined with replacement of fluid by continuous intravenous drip. This method tends to prevent the regurgitation of fluid, reduces abdominal distension and improves the patient's general condition.

In obstetrics nitrous oxide and oxygen are advised as the safest anæsthetic agents, but the services of an anæsthetist are required. Where economic reasons prevent this, preference is given to "gas and air" with Minnitt's apparatus. For the general practitioner who uses chloroform, Mennell's bottle is the safest.

The book is well illustrated, has a good index and is arranged in somewhat tabular form so that it is easy to read and simple to use for reference. This is a sound practical little book which will be read with interest, not only by the anæsthetist, but by the surgeon, obstetrician and general practitioner.

A TEXT BOOK OF SURGERY.

THE appearance of the fifteenth edition of "Rose and Carless Manual of Surgery" testifies to the continued popularity of this text-book.[1] The present edition differs from its predecessors in several important particulars. The bulky volume of earlier years has been replaced by two volumes of handy size, and since its appearance has synchronized with an historic event, this publication is issued as a "Coronation Edition" with specially prepared covers bearing the effigies of their Majesties and the Crown of England.

To mark the association of Lord Lister with the earlier editions of this book and with its original author, the dedication to this great surgeon, omitted from recent editions, has been restored.

In a review of the previous edition we emphasized in this journal the disadvantages attending the revision by one or two men of a text claiming to cover the whole realm of surgery.

This has been remedied in the present volumes by the collaboration of a large team, including representatives of American surgery; the result has been a very adequate revision, and further, more important changes and additions have been made than in any previous edition.

The American influence on the work is constantly obvious, and for Australian readers smooths over certain idiosyncrasies which we have learnt to associate affectionately with the London schools of surgery.

It augurs well for this work's continued popularity that almost every criticism made of the last edition has been fully met. Certain previous defects, such as inadequate treatment of the surgery of the sympathetic nervous system, have been remedied in such detail in this edition as almost to pass the bounds of an authoritative text-book of surgery.

It is also pleasing to note that in the section on fractures, the general tenor of treatment in earlier editions, which seemed to favour unduly the operative methods of treating closed fractures, has now come into line with modern practice.

It seems to us that for the next edition, which must soon be forthcoming, the section on abdominal surgery should be subjected to special scrutiny. There is a certain lack of proportion in the space allotted to various diseases, and in particular chronic duodenal ulcer seems to have been granted much less space than is warranted by its importance.

In the section on appendicitis the advice given may prove confusing to the student. The term catarrhal appendicitis is here used in a much wider sense than usual, and is held to include a condition of inflammation sufficiently extensive to produce a localized plastic peritonitis, with mass formation due to adherent omentum or coils of intestine, but without gross intraperitoneal suppuration. The remaining groups of appendicitis are defined as appendicitis with localized abscess, obstructive appendicitis, and appendicitis with diffuse or generalized peritonitis. In the paragraphs on treatment this first group is regarded as primarily a medical disease, and the advice to operate is limited to the following propositions: if in spite of suitable rest and medical treatment the symptoms, both general and local, are not commencing to abate at the end of forty-eight hours, operation should be undertaken, and still more so if conditions indicative of the formation of an intraperitoneal abscess are present. This may be good advice; it is certainly conservative advice, but we submit that it cannot be regarded as authoritative present-day opinion as to the treatment of acute appendicitis.

The operation is here delayed to a time at which there is much evidence that the surgeon should begin to stay his hand, and the insistence on signs of localized abscess-formation as an indication for immediate operation runs counter to the increasing published experience from many centres that operation under such conditions results in an unnecessary mortality, which can be reduced many-fold by a process of delay at this juncture. It is because of the general excellence of this book that we venture to criticize the author's unconventional attitude to the important surgical subject of appendicitis. In all other respects we have nothing but praise.

In its completeness, its attractive appearance, its modernity, and not least in its very moderate price, we can state without hesitation that in our experience this book has no rival among text-books of surgery. We again congratulate Dr. Wakeley and Dr. Hunter and the publishers on the continued success of their great text-book.

[1] "Rose and Carless Manual of Surgery for Students and Practitioners", by C. P. G. Wakeley, D.Sc., F.R.C.S., F.R.S., and J. B. Hunter, M.C., M.Chir., F.R.C.S.; Fifteenth Edition, in two volumes; 1937. London: Baillière, Tindall and Cox. Royal 8vo, pp. 1630, with 948 figures and 18 colour plates. Price: 30s. net.

The Medical Journal of Australia

SATURDAY, FEBRUARY 12, 1938.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

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THE DIDACTIC LECTURE.

ANY graduate worth his salt will continue to be interested throughout his life in the growth, politics and products of his university. Under the heading "University Intelligence" our readers are periodically acquainted with the decisions of university senates and councils, intramural appointments and developments. Less appears, however, about the undergraduate of today, yet it is his welfare, activities, problems and recreations which should provide an equal if not greater bond with his predecessor. His thoughts, decisions and communal strivings are recorded in other print than our own. There are now, for example, three recognized undergraduate periodicals at the University of Sydney, apart from the regular faculty journals which appear each term. One of these is described as the official organ of the Students' Representative Council, a democratic body, if one may use the term, the avowed purpose of which is to champion the common cause of the student community and to seek an improvement, if considered necessary, in existing or traditional conditions of study.

One important problem which has exercised this undergraduate parliament is the character and value of the set didactic lecture, with which most of us were so familiar. The monotonous reading of the same or almost identical lecture notes, for sixty minutes by the clock, to a jaded class results in a vicious circle whereby the lecturer himself becomes affected by the same boredom and reads more dully and mechanically than ever. Many of these lectures are completely unillustrated by either blackboard or wall chart. The notes are scarcely revised each year to encompass the ever-faster accumulation of medical facts. The provision of a bundle of foolscap, churned from the duplicator, in no way excuses such a lecturer from completeness or enthusiasm of description, even though it may represent a small sop to his conscience. The endeavour to include more and more recent work, without the critical preparation to scrap a corresponding amount of older, perhaps favoured material, at times results in a race between the clock and the lecturer's elocutionary capacity. So is confusion worse confounded. Things have apparently reached such a pass in some faculties that serious representations have been made to the students' council that the set lecture should be entirely abandoned and in its place a reversion to the individual tutorial system of the Old World universities be instituted.

Doubtless we can all remember without difficulty courses of lectures which might as well have never existed. We have shared with the student of today all the yawns, frowns and bewilderment of which he complains. But we can remember, too, lectures which were anticipated with pleasure and lecturers who were heard with satisfaction. These must exist today, though perhaps in thinner ranks. The speed of life has quickened. There seems to be less time to prepare a lecture thoroughly; the lecturer hurries to and from the theatre, or is himself fatigued before he begins. The art of public speaking has unquestionably declined in the last quarter of a century, and with it the capacity to attract and hold a student audience's attention for an hour of the clock. The fault, however, may not lie entirely with the lecturer. His task is always difficult. He has to contend with interruption caused by the late-comer, by a few noisy back-benchers on the look-out for any *double entendre*, or even by a stone-mason next door.

Where does the remedy lie? It rests with the individual lecturer. First, his lecture must be well prepared, logical and straightforward. Then he must come fresh, not tired, to the lecture, just as a surgeon is justifiably expected to approach the operating theatre. More important still, he must be enthusiastic. Genuine enthusiasm helps expression, is infectious and is projected over the class. He must insist on silence. If he doubts the power of his frown, he should resort to humour or even sarcasm. Silence helps the student to attend closely and helps the lecturer to think more clearly. Then, even if modern times have depreciated our power of vocal self-expression, they have brought certain most useful acoustic and visual aids to the lecture-hall. A medical lecture can scarcely be over-illustrated. Many lecturers who feel that they cannot part from the read lecture can do so readily if they have a sufficient number of lantern slides to guide them. These are better than epidiascopic projections of book-plates, because for them the theatre need not be so darkened that the student cannot write down a heading or two, and no pause occurs between two pictures. The power of the Ciné film is as great among students in a lecture-room as among the public in a cinema. Specimens, gramophone records, instruments *et cetera* all have a very important place, and medical lectures are few in which opportunity cannot be found to assist the spoken voice in this way.

The real purpose of the systematic lecture is often forgotten by the lecturer. It is not his task to encompass each fact and aspect of his subject. This is the function of the text-book. His real and most valuable duty is to guide the student's reading, to lay down and emphasize fundamental principles, and to illustrate them in a way which will appeal permanently to the mixed auditory and visual memory of his pupils. To this end many medical lectures by a little preparation can be illustrated by some actual clinical material, which helps so very much to impress certain facts upon a student's memory. One final caution: the lecturer must have an exact realization of the time factor and so dispose his subject matter that he is never hurried and yet finishes five minutes ahead of schedule.

Current Comment.

PROMINENT EYES.

K. B. NOAD has recently reviewed in a succinct and interesting essay, illustrated with reports of cases, the little understood subject of prominent eyes.[1] It is not unusual in discussions on prominent eyes to distinguish imperfectly between the ways in which the eyes may become prominent. Exophthalmos may be apparent or true. A further terminological aid to our conception of true exophthalmos would be a distinction between the condition in which the eyes are displaced forwards, and that in which the eyes "start forward", as if they were called passive exophthalmos and exophthalmos of central origin.

Apparent exophthalmos is seen unilaterally in congenital ox-eye (buphthalmos) and bilaterally in myopia, the eyeball being prominent because of its enlargement. Passive exophthalmos is seen bilaterally in oxycephaly, where premature synostosis of the base of the skull has caused the orbits to be too shallow to hold their natural contents: it is seen, usually unilaterally, when new-growth commences in the orbit (especially in chloromata, melanomata and optic nerve gliomata), when newgrowth metastasizes in the orbit (especially Hutchison's type of suprarenal tumour), and when newgrowth invades the orbit; it is seen when hæmorrhage occurs into the orbit, as in scurvy, or when inflammation occurs in the orbit or in the cavernous sinus. Under this head, too must come the "hard-boiled" eyes, eyes which are prominent as a natural characteristic without any accompanying disorder or as an accompaniment of obesity: in the former case the architecture of the skull produces the appearance; in the latter an increase in the orbital fat. Pulsating exophthalmos is a particular kind of passive exophthalmos due to vascular tumours of the orbit, including angiomata and aneurysms, or to arterio-venous aneurysm.

As Noad points out, the parallelism of the eyes is often disturbed when retrobulbar newgrowth displaces the eye forwards. This aparallelism of the optical axes should be distinguished from ocular displacement; for if the displaced eye is blind, as it sometimes is from optic atrophy, or if retinal correspondence is abolished, it will tend to squint, especially if there is pre-existing heterophoria.

The exophthalmos which often accompanies thyreotoxicosis is a phenomenon entirely different from passive exophthalmos, and its appearance is essentially different, the eye appearing to pop out of its socket and producing an expression of sudden violent emotion. Further, not only is the eyeball prominent, but nearly always spasm of the eyelids contributes to the staring expression. The patient is wide-eyed as well as pop-eyed. Many theories as to the mode of production of this form of

[1] *The Journal of the Old Sydney Hospitallers' Club*, December, 1937.

exophthalmos have been propounded and exploded. Even the obvious theory that the exophthalmos results from the stimulation of structures supplied by the sympathetic nervous system has been assailed on the ground that it has not disappeared on section of the sympathetic pathway; but it would be just as logical to attempt to abolish arterial supertension by splanchnic neurectomy after degenerative vascular changes had set in. No doubt anatomical changes occur in the orbit, as has frequently been postulated to explain the slight and slow improvement in exophthalmos after thyreoidectomy. The morbid anatomy of exophthalmos needs much further study. One of Noad's patients who had exophthalmos without thyreotoxicosis was operated upon by Douglas Miller, and was found to have greatly hypertrophied extrinsic ocular muscles, which occupied many times their normal space.

The initial causal mechanism of exophthalmos is probably not that which maintains exophthalmos. Our understanding of the pathogenesis of exophthalmos of central origin is made clearer by the variations that sometimes occur: it may be unilateral, or, if bilateral, may be unequal; on one or both sides there may be palpebral ptosis instead of lid retraction. Again, exophthalmos may occur without thyreotoxicosis in topical disease of the brain, where there is good reason to believe that the upper midbrain is the seat of the disease, and it may be associated with the same variety of ocular and palpebral symptoms.

THE CAUSE OF PULSUS ALTERNANS.

TRAUBE described the phenomenon of alternation of the pulse nearly seventy years ago, but its cause is still obscure. There can be no question of its importance in clinical medicine, and with certain reservations it is of grave prognostic import. Sometimes a regular alternation of stronger and weaker beats may be observed in conditions which are only transitory, such as severe fevers, or bouts of tachycardia; but it is notorious as being of evil omen in cases of myocardial degeneration. The failing hypertensive heart not infrequently shows alternation, though the routine use of the sphygmomanometer has perhaps revealed more instances than were once suspected, and has thereby corrected the unduly pessimistic view once held of this sign. It is possible for patients with this condition to make a temporary recovery, though, once it is discovered, the verdict undoubtedly must be grave. Louis N. Katz and Harold S. Feil have made a careful study of five patients with *pulsus alternans*, using ordinary clinical observations together with simultaneous graphic recordings of the electrocardiogram, subclavian arterial pulse and the heart sounds.[1] These optical methods afford the opportunity of making exact measurements of the changes that take place, and have in this instance led the authors to the view that alternation is in the main due to dynamic fluctuations in the circulation depending on variations in the systolic residue of blood. In general, two theories have been advanced: one of these favours occurrence of such rhythmic variations in the circulation; the other attributes the phenomenon to failure of certain portions of the ventricular muscle to contract owing to prolongation of the refractory period. The study of the optical records shows the alternation very plainly, especially in the graphs of the arterial pulse, and this is the more striking since the electrocardiogram, as is usually the case, exhibits little change from beat to beat. In some of the records it can be plainly seen that the smaller beats arise from a higher level than do the larger beats, indicating a greater degree of arterial distension and therefore a higher diastolic blood pressure. Alternation of the heart sounds is also demonstrable. It is, of course, well recognized that alternation of the pulse is most simply and convincingly demonstrated at the bedside by the sphygmomanometer, though alternation of the heart sounds, in particular the second sound, may also be picked up. On examination of the measured records, Katz and Feil found that alternation of the pulse itself was associated with some rhythmic variation of the intensity of the heart sounds, in the duration of the isometric and ejection phases of the cardiac cycle and in the pulse gradient; but the duration of the systole and its previous diastole were not changed consistently. Conduction changes were found in the electrocardiograms in four of the five cases; but, as remarked above, no alternation in electric potential of the contracting heart was observed. The authors, after a thorough discussion, admit that they cannot exclude variations in the refractory phase of the heart muscle as being an underlying cause of alternation. This may be an important factor in initiating and perpetuating *pulsus alternans*; but they think that sudden changes in rhythm, such as occur with respiratory disturbances, extrasystoles or even sinus arrhythmia alter conditions of volume and tension so as to establish alternate variations in the systolic blood residue. Once started, these alternations tend to continue. All this may seem academic and dry; but really it tends to emphasize how in this interesting condition there is, as it were, a sinister interference with some of the primal dynamic factors governing the customary striking regularity of the circulation. Whether or not the practitioner of medicine cares how it is produced, he should at least be on the alert to recognize *pulsus alternans*. As Katz and Feil point out, it is of serious import, and more particularly when it occurs when the heart is relatively slow, when it is readily produced by otherwise unimportant irregularities, such as extrasystoles, and especially when it tends to persist long. Finally, it may be remarked that, like most ominous signs of cardiac disease, it may be readily recognized by any careful observer by simple means, in this case with a sphygmomanometer, just as gallop rhythm may be observed by using a stethoscope.

[1] *The American Journal of the Medical Sciences*, November, 1937.

Abstracts from Current Medical Literature.

SURGERY.

Ingrown Toe-Nail.

C. J. HEIFETZ (*American Journal of Surgery*, November, 1937) reviews the subject of ingrown toe-nail, and after discussing numerous methods of treatment presents two procedures as a basis for treatment. In the early stage, when the lesion is accompanied by early inflammation of the nail wall, a small pledget of cotton wool soaked in alcohol is inserted between the edge of the nail and the soft parts in such a way as to allow some of the wool to project over the end of the nail edge. This is done by pulling the soft parts away from the nail so as to expose the edge, and inserting a thin wick of cotton wool with the flat end of a small probe. The excess alcohol is wiped away and a little collodion is applied to the area and the wool. Following this treatment the patient is instructed in the proper method of trimming toe-nails, and a house slipper or proper shoe is worn. The patient returns in one week and this treatment is repeated at weekly intervals until the corner of the nail has grown sufficiently to make its embedding improbable. If the nail corner is trimmed very closely when the patient is first seen, daily or bi-daily foot baths are used for a week or so until there is a sufficient growth at the corner of the nail to carry out the procedure. The procedure outlined above is usually painful. In the second stage, when there is discharge from the area due to more advanced inflammatory changes, the patients are given the option of the above conservative treatment or operation. If the patient is first seen in this stage with a closely trimmed nail, operation is unequivocally recommended. In the third stage, when granulation tissue is present, operation is always advised. The operative procedure is as follows. The foot is prepared for three to five days by hot foot baths twice a day, and a cut-out shoe is worn. Under block anæsthesia and after application of a tourniquet, an incision three-eighths of an inch long is made in the eponychium and proximal nail wall, extending slightly diagonally and laterally from a point on the nail corresponding to the line on which the nail will presently be excised. This incision is made deep enough to strike the root of the nail. Medial and lateral flaps are dissected along this line so as to expose at least the lateral third of the nail root on that side. The lateral flap should also include sufficient tissue to expose the embedded nail edge. The nail is then split longitudinally over a thin spatula and the lateral portion is removed. The underlying matrix is curetted thoroughly and then carbolized. Simple dressings are applied, and the patient may go to work the next day. The dressings are changed every few days, and after the first few days the edges are brought towards each other by strips of adhesive plaster.

Treatment of Abdominal Distension.

M. S. WEINBERG (*American Journal of Surgery*, November, 1937) considers that abdominal distension is primarily an atonic condition of the musculature of the gastro-intestinal tract with increased secretion of fluid from the mucosa causing more pressure from within, accentuating the atony and forming a vicious circle. Continuous duodenal drainage removes the increased secretions and allows the gastro-intestinal walls to return to normal, so that peristalsis can be produced as the result of normal stimuli. Suction is obtained from a simple water-drip apparatus, and this prevents vomiting and makes the patient comfortable. Even when central stimulation with agents such as pituitary extract fails, continuous duodenal drainage is often successful. The return of peristalsis is indicated by an increase in the amount of fluid taken by mouth over that returned through the duodenal tube.

Subphrenic Vagotomy for Duodenal Ulcer.

ASHER WINKELSTEIN (*Journal of the Mount Sinai Hospital*, November, 1937) reports two cases of duodenal ulcer which were treated by section of the left vagus nerve in addition to gastro-jejunostomy, and in which the patients were followed for seven and four years respectively. The post-operative clinical course was strikingly good. Gastric hyperacidity and hypersecretion, which in duodenal ulcer appear to be due to nervous factors acting through the vagus, were abolished; in one case the acid secretion returned to normal only in the seventh year. A report of 28 cases of left vagotomy in conjunction with partial gastrectomy is promised.

Injection Method of Treating Hernia.

C. G. BURDICK AND B. L. COLEY (*Annals of Surgery*, September, 1937) present conclusions from a study of 66 patients with hernia treated by the injection method since 1934. Several solutions were tried, but none was found to have any special advantage over the others. Comparatively few sequelæ occurred, the patients tolerating the injections well. Full precautionary measures were taken, and patients wore trusses continuously during the treatment as advocated. Immediate results were gratifying in that the impulses disappeared and, generally, for a time no definite evidence of the existence of a hernia was present. This brief period of relief would commence after five or six injections and would last possibly for three or four months, particularly if an injection was given occasionally during this period. However, in 47 of the 56 cases followed, a relapse was noted, usually by both the patient and the doctor; so that at present only eleven patients are apparently cured, and nine of these are still wearing trusses. From conditions found at operation on several patients previously treated by injection the belief is held that it is extremely difficult to deliver the solution to the exact spot needed for the obliteration of the sac, and even when the solution does cause a temporary proliferation which either obliterates the sac or masks the impulse on coughing, this tissue reaction is gradually absorbed or diminishes until a state is reached approximating to that which existed prior to the injection. Some scarring may persist, but it is questionable whether this scarring strengthens the defence against a hernia, except when it causes an obliteration of a narrow sac in a person whose muscles and fascia are otherwise normal.

Fascial Suture Operation for Hernia.

C. G. BURDICK, D. H. M. GILLESPIE AND N. L. HIGINBOTHAM (*Annals of Surgery*, September, 1937) review the end results of 1,485 fascial suture operations for the repair of all types of hernia. Infections were found to be more common in herniæ repaired with fascia than in those in which other forms of suture material were used. The incidence of infection was greater when non-autogenous fascia (12%) than when autogenous (8%) was used. The number of recurrences was discouraging, although it must be borne in mind that fascial repair is reserved for the more difficult types of hernia. The introduction of a large needle through the transversalis fascia and Poupart's ligament frequently left a weak spot which predisposed to recurrence. In many of the secondary operations no trace of the previously used fascial sutures could be found.

Acute Osteomyelitis of the Upper End of the Femur.

RANDOLPH JONES, JUNIOR, AND LOUIS ROBERTS (*Surgery, Gynecology and Obstetrics*, December, 1937) present a *résumé* of the historical, anatomical and pathological aspects of acute osteomyelitis of the head of the femur. They report seventy-one patients treated during the period 1930-1936, six of whom were under the age of two years. They point out the difficulty in making a diagnosis in the early stages of the illness, and give the following reasons: (i) The infection originates in a bone covered by a large muscle mass. (ii) The child is often unable to localize his pain to a small area and may refer it to the general region of the hip, the thigh or the knee. (iii) The examiner frequently cannot demonstrate bone tenderness and may find it difficult to eliminate the numerous disorders which simulate primary involvement of the upper end of the femur. (iv) The clinical picture of a lesion which begins in the metaphysis of the neck

and which is complicated by early infection of the hip joint, differs from that presented by a patient with a primary focus in the metaphysis opposite the greater or lesser trochanter, which does not extend to cause a pyarthrosis of the hip. The authors emphasize the value of aspiration of the hip joint as an aid to diagnosis and at the same time as an aid to determining the extent of the infection. They suggest the introduction of a large calibre needle under local anæsthesia along the anterior surface of the neck of the femur until the joint space is entered, and the examination of the aspirate by smear and culture. The presence of pus or organisms indicates that infection of the joint is present, and the severity of the involvement may be gauged by the type of exudate. The absence of purulent fluid from the exudate, however, does not exclude acute osteomyelitis of the hip. The presence of pneumococci, gonococci or streptococci in the hip joint suggests a probable primary hip joint infection, although streptococcal pyarthrosis may be secondary to acute streptococcal infection of the bone; if *Staphylococcus aureus* is found in the joint, there is probably a focus in the adjacent bone. Under the heading of treatment the authors lay stress on the fact that early diagnosis secures a better end result in all types of lesion. The toxæmia may be combated by a blood transfusion and by the use of antiserum (staphylococcal antitoxin), and their local treatment consists in drilling holes through the neck to the capital epiphyseal line. If pus is encountered the drill hole is enlarged, or if the abscess is superficial the cortical bone is removed with a rongeur until adequate drainage is obtained. If a frank pyarthrosis of the hip is present, the joint is drained with a rolled strip of tubing. During the post-operative period the authors recommend skin traction followed by immobilization in a hip spica until evidence of bone healing is present.

Experimental Production of Goitre.

HOWARD R. MAHORNER (*Archives of Surgery*, November, 1937), using dogs and guinea-pigs, has attempted to produce goitrous changes in the thyreoid gland of dogs and guinea-pigs by means of infection, injury to and freezing of the adrenal glands, and by the intraperitoneal injection of the anterior pituitary-like gonadotropic substances obtained from the urine of pregnant women, and the intraperitoneal injection of anterior pituitary extract. The infection was introduced directly into the gland by means of frankly contaminated foreign bodies, and the injury to the adrenals was produced in some animals by crushing with an artery forceps and in others by spraying with ethyl chloride. The author concludes that: (i) Infection has no specific effect on the histological picture of the stage of activity of the thyreoid gland or on the size of the gland. (ii) Injury to or freezing of the adrenal gland results in no gross or microscopic changes in the thyreoid gland. (iii) Anterior pituitary-like gonadotropic substances obtained from the urine of pregnant women have no effect on the histological structure of the thyreoid gland when injected daily over varying periods of time. (iv) An extract of the anterior lobe of the pituitary gland produces a histological picture in the thyreoid gland which may be interpreted as increased activity of the gland, namely, disappearance of colloid or diminution of the amount of colloid in the acini, an increase in the size of the epithelial cells, which change from low cuboidal to high columnar epithelial cells, and an increase in the number of vacuoles in the colloid. (v) Calcium chloride, when added to drinking water, produces changes in the thyreoid gland of animals which have been on the regimen eighty days or longer. The microscopic changes are similar to those described as the result of the administration of anterior pituitary extract.

Asymptomatic Appendicitis.

H. J. SHELLEY (*Archives of Surgery*, October, 1937) has made a study of asymptomatic pathological conditions of the appendix. He has based his study on 2,065 consecutive appendicectomies performed during abdominal operations, the indications for which were in no way associated with the appendix. Of the appendices removed, 1,904 were examined microscopically, and the author presents his findings in tables and charts. One-third of the appendices were either normal or relatively normal. In just less than one-third "slight to moderate, but definite, inflammation (a simple chronic appendicitis)" was present. In over one-third of the cases there was evidence of pronounced pathological change. In this group were the more acute types of appendicitis, together with those in which atrophic changes were present and those in which the following pathological changes were found: oxyuris in the lumen, mucocele, tuberculosis, diverticulum, hyperplasia of the mucosa, and tumours. In 62% of cases inflammatory changes were found in the absence of a history or of physical findings indicative of a pathological condition in the right lower abdominal quadrant. A slight but definite inflammatory change in the appendix occurs in the presence of inflammation elsewhere in the abdomen. This becomes pronounced in the presence of chronic suppurative and acute salpingitis and of peritonitis. Acute appendicitis, even with actual suppuration, can exist without any subjective or objective evidence of its presence; the incidence in this series was 1·7%. The author made a study of cases in which the gall-bladder was removed, and found that there was no increase in the incidence of cholecystitis in the presence of appendicitis. He concludes from this finding that the positive statement can be made that there is no evidence to indicate that inflammation of the appendix causes inflammation of the gall-bladder. With increasing age there is an increase in the incidence of atrophic and inflammatory changes in the appendix. This is most pronounced with chronic obliterative appendicitis. It does not hold true for periappendicitis, which is caused by conditions prone to occur in early and in early middle life. The author points out that in his series the incidence of pathological change other than inflammation is very low. This indicates that these other conditions as a rule produce symptoms referable to disease in the appendix. The incidence of post-operative conditions was found to be no greater than would be expected in a similar list of operations in which appendicectomy was not performed. There was, moreover, no increase in mortality. The author concludes that the incidental removal of the appendix is a safe and worthwhile procedure.

Diverticulosis.

P. W. BROWN AND D. M. MARCLEY (*The Journal of the American Medical Association*, October 23, 1937) discuss the prognosis of diverticulosis and diverticulitis of the colon after review of a large series of patients. It is not possible to state what percentage of patients suffering from diverticulosis will develop diverticulitis. Follow-up data were obtained in 86% of a series of 596 cases of diverticulitis or diverticulosis. In a few cases of simple diverticulitis complications may develop and require surgical treatment. Surgical treatment was employed in 99 cases of diverticulitis; 57 of the patients were cured and 43% either continued to have intestinal trouble or died after the operation. A peculiar predestination seems to occur in cases of diverticulitis; symptoms may be entirely absent or they may be moderate or severe. It is impossible to say how many patients who have diverticulosis will suffer later from complicated or uncomplicated diverticulitis. Medical treatment of diverticulitis consists in rest, the application of heat, regulation of the diet and the oral administration of olive oil. In 63% of cases this type of treatment was successful, but in 37% of cases the results were only moderately good or poor. However, many of the latter group of patients were able to live in comparative comfort. The results of the authors' observations confirm previous opinions that the relationship between diverticulitis and carcinoma of the colon is probably incidental rather than actual. In a third of the cases of diverticulitis the symptoms are the result of inflammation, and in two-thirds of the cases the symptoms are the result of obstruction and inflammation. The authors give a full plan of non-operative treatment of diverticulitis.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at Ballarat on November 27, 1937, the convenor of the Science Subcommittee, DR. A. E. COATES, in the chair. The afternoon meeting was held at the Ballarat Base Hospital and took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. Part of this report appeared in the issue of February 5, 1938.

Tuberculous Disease of the Spine in an Elderly Man.

DR. GEOFFREY PERN showed a male patient, seventy-two years of age, a manual worker in the local gold mines, coming of a family in which longevity was the rule. Four or five years earlier he had for eighteen months suffered from giddiness and lassitude, which had decreased after dental extractions. At the beginning of 1937 night sweats and fever had started, and the patient had had pain and stiffness in the back, chiefly in the lumbar region, and radiating round both sides of the trunk. He had been able to get relief by leaning to the side opposite the painful one. Six weeks before the meeting his legs had become progressively weaker until he was unable to walk. He had a feeling of unawareness of what his legs were doing, and it was to this feeling that he ascribed his inability to walk. One week before the meeting an indwelling catheter had been introduced because of dysuria. On the day of the meeting the patient had informed Dr. Pern that when he coughed or sneezed his body felt about to break in halves. In his early days the patient had had gonorrhœa, which had been inadequately treated, and a chancre, which had been treated by a pharmacist. For a long time he had been subject to abdominal pain, with flatulence and heartburn. Dr. Pern said that as the patient had been in the hospital for two days only, the investigation was necessarily incomplete. The systolic blood pressure was 120 and the diastolic blood pressure 75 millimetres of mercury. Merely negative findings had been recorded on examination of the heart, lungs and abdomen. The patient had control of defæcation, though the left side of the prostate gland was enlarged. The spine curved backwards, particularly at the level of the eighth thoracic spinous process, but there was no localizing tenderness. Dr. Pern had examined the nervous system very carefully. The man was of normal intelligence and no abnormality of the cranial nerves was demonstrated. The musculature was fairly good and no wasting was obvious. There was weakness in the maintenance of posture in the legs, but not in the arms, and passive movements were normal. Flexion of the trunk caused pain. The abdominal muscles were weak and the left leg was paresed more than the right, with definite asynergia. The sensory response to light touch was present but impaired from the umbilicus down. There was a zone of pain and hyperæsthesia from the level of the umbilicus upwards to the costal margin, and a zone of anæsthesia at the level of the umbilicus. The sense of localization was fairly good, and that of discrimination between heat and cold, though impaired, was present. There was a small area on each buttock and on the lateral side of each foot in which hyperæsthesia was present. The reflexes in the arms were normal, the abdominal reflexes were absent, the knee jerks were active but the left one was weak, the ankle jerks were present but weak, the plantar reflexes were extensor in character, and the pupillary reactions to light and accommodation were normal. The vibration sense was absent over the external malleoli and weakly present over the extremities of the femora, and the sense of position, though normal in the right, was absent in the left great toe. An examination of the blood film and of the cells had been made with negative results, and the report on the reaction of the blood serum to the Wassermann test was not then available. There was diminution of pressure of the cerebro-spinal fluid, and in the Queckenstedt test there had not been much rise in the manometer on pressure over the jugular vein, but there was a greater rise when the patient had coughed. The cerebro-spinal fluid was clear and colourless, and no excessive number of cells were present; the chloride content was low, the globulin content was greater than normal, and the total protein was very high, amounting to about 0·1%. In the skiagram was shown a regular area of rarefaction with collapse of the bodies of the seventh and eighth thoracic vertebræ with angulation and a definite degree of coalescence, and in addition some degree of lipping of the lumbo-sacral vertebræ was evident.

DR. THOMAS KING said that the condition was tuberculous disease of the spine. Senile tuberculous disease of bone occurred in the spine, in the knee or in the wrist more commonly than elsewhere in the body. There was an abscess present in the case of Dr. Pern's patient, which was the cause of the paraplegia. The shadow of this abscess could be detected in the films. Dr. Pern had informed Dr. King that he was going to have the chest examined radiographically. The treatment advocated by Dr. King was hyperextension of the spine on a plaster bed with general measures directed to the improvement of health.

DR. C. FARRAN-RIDGE agreed that the paraplegia was due to pressure.

DR. W. R. ANGUS sought information about the treatment of the abscess, and asked whether it should be aspirated and whether Coley's fluid should be injected.

DR. C. J. O. BROWN agreed entirely with the diagnosis, and stated that the treatment of secondary paraplegia was almost always rest with some hyperextension, in the hope that the condition would settle down. Attempts to aspirate the abscess were contraindicated. Aspiration of these abscesses was always difficult, and attempts were more likely to cause complications than to relieve pressure symptoms. Laminectomy used to be performed, but it was usually unsuccessful and unnecessary.

DR. A. E. COATES said that Dr. Pern's patient presented an excellent illustration of a transverse lesion of the cord. There was a band of anæsthesia around the umbilicus with a hyperæsthetic area above it. The motor system had suffered more than the sensory system, though the signs of the upper motor neurone lesion had not caused as much spasticity as one would have expected. He suggested that it would be of interest to carry out the test in which the examiner traced letters or numbers on the abdominal wall or legs of the patient to test whether the patient could identify the letters or numbers. Dr. Coates agreed that the proper orthopædic treatment had already been outlined and that aspiration of the abscess would be wrong. It was the thickening and the accumulation of tuberculous detritus that caused pressure rather than the pus. The canal was narrow in the thoracic region, and this fact was responsible for the frequency with which this site was affected first by the pressure. Dr. Coates then advocated conservative treatment for the bladder condition. There had been a swing away from attempting to keep the bladder empty. The orifice always opened before the bladder burst. Expression of urine from the bladder by suprapubic pressure was preferable to catheterization. Pyelonephritis was the condition which was to be feared most. The finding by Dr. Pern that the protein in the cerebro-spinal fluid was greatly in excess of the normal amount was in keeping with the presence of pressure on the cord.

Retroperitoneal Adeno-Carcinoma.

On behalf of DR. N. A. LONGDEN, DR. F. P. SMITH showed an aboriginal woman, aged forty-one years, who had walked into the casualty department of the hospital and had complained of pain in the right hypochondrium. A palpable tender mass had led to the provisional diagnosis of acutely inflamed gall-bladder on her admission to hospital. The cholecystograms had been normal, but in the plain skiagram the presence of a mass below the

liver and kidney was demonstrable. At laparotomy the mass was exposed; it was found to be retroperitoneal, and extended over to the left hypochondrium and appeared to arise in or behind the hepatic flexure of the colon. It felt like a mass of fairly adherent glands, and when a portion was opened it was found to contain jelly-like material which had reminded Dr. Smith of filariasis. By means of a barium meal a filling defect above and behind the hepatic flexure had been seen. The condition appeared to be a colloid forming adeno-carcinoma of a very malignant nature, and at the operation it had not been possible to make certain whether it had arisen from a primary lesion in the colon.

DR. C. J. O. BROWN said that a few weeks earlier he had seen a parallel case at the Alfred Hospital, with the diagnosis of cholelithiasis and anæmia. The patient was tired and very pale; the red blood cells numbered 3,000,000 per cubic millimetre; the patient had pain in the right hypochondrium, and what appeared to be a large gallstone could be seen in the skiagram. The anæmia did not decrease while the patient was in the medical ward, and the mass developed until it could be localized definitely in the right loin. On the assumption that the mass was renal a pyelogram was prepared, but was of normal appearance. The patient died, and at the autopsy a carcinoma of the ascending colon was found, although during life a barium meal revealed no abnormality. Dr. Brown was inclined to think that the aboriginal woman had a colonic tumour.

Carcinoma of the Breast.

Dr. Smith also showed on behalf of Dr. Longden a woman, aged fifty-one years, who had had three children, the youngest of whom was only two years of age. For three months the woman had had a tumour in the left breast; during that time it had increased in size from that of a walnut in the lower and outer quadrant until it occupied almost the whole of the outer half of the breast, while a very large area of *peau d'orange* and glands could be felt in the axilla.

DR. VICTOR STONE discussed the relationship of surgery and radium therapy in the treatment of this type of lesion. Having approached this subject primarily as a surgeon and also as a radiotherapeutist, he considered that both forms of treatment were needed in practically every case of carcinoma of the breast. The woman shown would be classed as a typical advanced case, with *peau d'orange* supraclavicular and axillary glands. Radical mastectomy was not suitable at present. In the case of a patient sent for radium therapy at the Royal Melbourne Hospital recently, the condition was even more advanced and fungation had commenced. The problem presented by the patient shown was the prevention of fungation and of foul discharge. Dr. Kaye Scott's plan of campaign for the patient at the Royal Melbourne Hospital would be suitable in the case under discussion. The first stage consisted in complete irradiation of the tumour and of the gland fields, though preliminary radiography of the chest was essential. The tumour would decrease in size and the skin would become flat and hard. The glands in the axilla would shrink and post-radiational fibrosis would terminate lymph permeation and thus stop the spread of the carcinoma. Three months afterwards, Dr. Stone said, he would advocate surgery alone in the second stage of treatment. Others might say that radon needles should be implanted. He would suggest simple removal of the breast and breast tissues, with or without the pectoral muscles. Radium therapy did not make surgery more difficult nowadays, though the amount of hæmorrhage was decreased by it. The operation then would consist in mastectomy, removal of the pectoral muscle perhaps, and of any glands in the axilla that came out conveniently with the deep pectoral fascia. The third stage of treatment was undertaken two or three weeks after the wound had healed. It consisted in complete irradiation of the whole field. There was a choice between the implantation of radium or of radon needles. The needles were implanted mathematically 1·7 centimetres apart, and the position of the needles was checked up subsequently by radiography. If after a day or so it was considered necessary, an extra needle could be introduced where it was required. In any case the prognosis was doubtful, and microscopic secondary deposits were probably already established well beyond the area; but it was possible to prevent ulceration and fungation and to make the patient's death a much cleaner and happier one.

DR. A. E. COATES was not prepared to agree with those who considered that simple removal of a breast for carcinoma was as good as complete radical mastectomy; if the surgeon used diathermy to control bleeding from the perforating vessels and attacked from the lateral aspect, turning everything medially, radium therapy previously applied did not inconvenience the surgeon and the operation was much less bloody than simple mastectomy.

Streptococcal Empyema Treated with "Prontosil".

Dr. Smith stated that he had been impressed with a report he had read in *The British Medical Journal*, of the treatment of streptococcal empyema with "Prontosil" used intrapleurally. In the report it was stated that thick pus became thinner and three days later was sterile, and that rib resection had been avoided by this treatment. He showed a girl whom he had treated along these lines at the Ballarat Hospital. She had had attacks of pneumonia in July and August, 1937, and again towards the end of October she had had acute right basal pneumonia with distant tubular breathing and pain over the affected area. Two days after the continuous high temperature ceased he had needled the right base because the temperature was again rising, and had obtained a quantity of straw-coloured fluid. Gram-positive cocci resembling streptococci were seen in the film, a culture of which resulted in the growth of almost pure streptococci. The girl became very ill and was treated with "Cardiazol" and "Ernutin", which were injected frequently. On the following day, October 30, the chest was examined radiographically, and a dense area was found over the base of the right lung. On October 31 Dr. Smith had again needled the chest and had introduced five cubic centimetres of "Prontosil" intrapleurally. On culture of the fluid a pure growth of non-hæmolytic streptococci was obtained in forty-eight hours. When he had next needled the chest on November 8 the fluid in the first syringe was orange-coloured, as was the fluid in the second syringe, but the third syringe contained thick, heavy pus, from which non-hæmolytic streptococci were grown in pure culture. On November 10 Dr. Smith aspirated the chest, taking off fifteen ounces of thick pus with Potain's aspirator. On November 15 an operation for rib resection was performed with closed drainage, and open drainage had been used since November 19. Though drainage from the chest was still continuing, the general condition of the patient had improved and was satisfactory at the time of the meeting. Dr. Smith said that his object in showing the patient was to point out that in this case the introduction of "Prontosil" had not caused the pus to become thinner or sterile and that the rib resection operation had not been avoided. He invited a discussion on the method of treatment he had used, and said that he would be interested to hear of the results in the hands of other people.

DR. STANLEY WILLIAMS said that much had been published on the actions of numerous chemotherapeutic substances, including the soluble sulphonamides, the use of which had been advocated for streptococcal infections in the blood stream and for puerperal sepsis. He had the impression that the substances must be given into the blood stream and that they did destroy organisms in the blood stream, and he considered that, used in this manner, "Prontosil" had been proved to be of value.

DR. C. J. O. BROWN said that he used closed drainage for empyema. It hastened expansion of the lung, and in synpneumonic empyema it was the only safe method of drainage. It was very hard to keep the attachment watertight for longer than a week or ten days. He also washed out the chest with eusol at the time of operation. The only doubt he had about this procedure was the possibility of the production of pleural shock. A resident medical

officer at the Alfred Hospital had washed out a typical empyema cavity, and a week later the patient had had pains followed by paresis in the left shoulder, which had been accounted for on the assumption that it was due to a small cerebral embolus, possibly an air embolus. Dr. Brown wondered whether the so-called pleural shock was really an embolic phenomenon.

DR. GEOFFREY STRAHAN pointed out that patients were usually able to overcome the generalized infection in gonorrhœa, but the fact that the condition got a local hold rendered it difficult to eradicate. By dilatation and stirring up of the local foci the reaction of the tissues could be stimulated with beneficial results.

Tuberculosis in Pregnancy.

DR. W. R. D. GRIFFITHS outlined the case notes of a woman, aged twenty-six years, who had come under his care at the hospital on account of excessive vomiting during pregnancy. The last menstrual period was from September 8 to September 14, so that she was about two months pregnant. It had been known for some time that she had pulmonary tuberculosis, and on March 11, 1937, the sputum contained tubercle bacilli. She had granular foci of tuberculosis at both apices and in the middle lobe of the right lung. The excessive vomiting had been going on for over three weeks, but the tuberculous process seemed to be decreasing. Recent radiographic examination of the chest confirmed the previous ones, but did not indicate any advance in the process, and the patient had not been producing sputum recently. The urine had been examined, and though it contained acetone bodies, the tests for albumin gave negative results. The patient herself, like other members of her family, was not intellectual, and the family was a very prolific one. Dr. Griffiths said that he would like to hear a discussion on the advisability of the induction of abortion in the case of this patient. If abortion was considered desirable, he wondered whether she should also be sterilized; and if she should be sterilized, he would like to hear some opinions concerning the most suitable method of sterilization to adopt. His own opinion was that the best thing to do was to carry out a miniature Cæsarean section. He believed in the rules that if a tuberculous subject was a virgin she should not marry, if she married she should have no children, and if she had a baby lactation should be prevented as soon as possible.

DR. E. J. HANLY said that he was afraid that Dr. Griffiths was allowing his views on sociology to influence his medical views. He considered that the right thing to do was to leave the patient alone to continue her pregnancy. Apart from the important fact that Dr. Griffiths was proposing the destruction of a human being, there was a French school that had shown that more harm was done by interference.

DR. W. T. GREENING referred to the fact that pregnancy usually increased the activity of tuberculosis as a fact which had been enunciated at the time when subjects of pulmonary tuberculosis were poorly treated, and that the treatment by abortion had developed in that period. He thought that if the patient could be looked after properly the prognosis nowadays was not nearly so unfavourable. He instanced a case of his own in which pregnancy had not affected the prognosis, although the patient was a diabetic subject undergoing insulin treatment. He suggested that Dr. Griffiths should induce a pneumothorax and let the pregnancy continue.

DR. SYDNEY PERN suggested that the improvement in health of a pregnant tuberculous woman was associated with the increased absorption of calcium salts during pregnancy. As calcium absorption was so important in the treatment of tuberculosis, Dr. Griffiths might make use of the period of pregnancy to saturate the patient with calcium.

DR. JAMES said that he had referred this patient to Dr. Griffiths from the chest clinic. She had refused sanatorium treatment and had not allowed him to induce a pneumothorax. He did not considered, therefore, that she was receiving proper attention for tuberculosis. He was satisfied that she could go through the pregnancy quite well, but it was very probable that the tuberculous process would light up with renewed activity after the birth of the baby. In the circumstances, if anything had to be done to terminate the pregnancy, it had to be done at an early date.

DR. D. O. BROWN said that he was sure that, if they had been present, authorities such as Dr. Bell Ferguson, Professor Marshall Allan or Dr. Arthur Wilson would have advised termination of pregnancy in the case of Dr. Griffiths's patient. A patient who had had severe tuberculosis could not be regarded as cured till safely dead. He would recommend the termination of the pregnancy, and thought that the patient should be strongly advised against further pregnancy.

DR. W. SLOSS said that he had had a number of patients with pulmonary tuberculosis who had improved while pregnant and had gone to full time, but most of them had died within six months of confinement.

DR. W. RAWLINGS said that he thought the decision depended on whether the patient was going down hill. If the patient was progressing favourably he thought the pregnancy should be terminated, but if progress was unfavourable he would prefer to let the pregnancy continue because of the mental outlook of the mother, who would probably have a greater desire to live for the sake of the baby, or would be more resigned to die if before doing so she gave birth to a live baby.

(To be continued.)

NOMINATIONS AND ELECTIONS.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Perkins, Richard Basil, M.B., B.S., 1936 (Univ. Sydney), 12, Parkview Road, Manly.

The undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Agar, Wilfred Talbot, M.B., B.S., 1934 (Univ. Melbourne), Commonwealth Serum Laboratories, Parkville.

Clough, James, M.B., B.S., 1936 (Univ. Melbourne), 334, Wattletree Road, East Malvern.

Dallimore, George Menzies, M.B., B.S., 1929 (Univ. Melbourne), Rutherglen.

Gild, Jack Lawrence, M.B., B.S., 1937 (Univ. Melbourne), 9, Melby Avenue, St. Kilda.

Gorr, George, M.B., B.S., 1937 (Univ. Melbourne), Base Hospital, Warrnambool.

Hayden, Francis Joseph, D.G.O. (Melbourne), M.C.O.G., F.R.C.S. (England), 55, Collins Street, Melbourne.

Hellings, Brian Lister, M.B., B.S., 1937 (Univ. Melbourne), 108, Esplanade, Brighton, S.5.

Hopkins, Charles, M.B., B.S., 1934 (Univ. Melbourne), Eye and Ear Hospital, East Melbourne.

Love, George Cross, M.B., B.S., 1937 (Univ. Melbourne), 2, Rockbrook Road, East St. Kilda.

Millar, John Patrick, M.B., B.S., 1935 (Univ. Melbourne), Austin Hospital, Heidelberg.

Murphy, Ian Stephen MacLeod, M.B., B.S., 1937 (Univ. Melbourne), c.o. The Ballarat Trustees Company, Ballarat.

Pilkington, Ralph, M.B., B.S., 1937 (Univ. Melbourne), 59, Cole Street, Elwood.

Sawrey, Clifford Ernest, M.B., B.S., 1937 (Univ. Melbourne), 141, Normanby Road, Caulfield.

Smith, Edgar Francis John, M.B., B.S., 1937 (Univ. Melbourne), Royal Melbourne Hospital, Melbourne.

Watters, George Graham, M.B., B.S., 1933 (Univ. Melbourne), Alfred Hospital, Prahran.

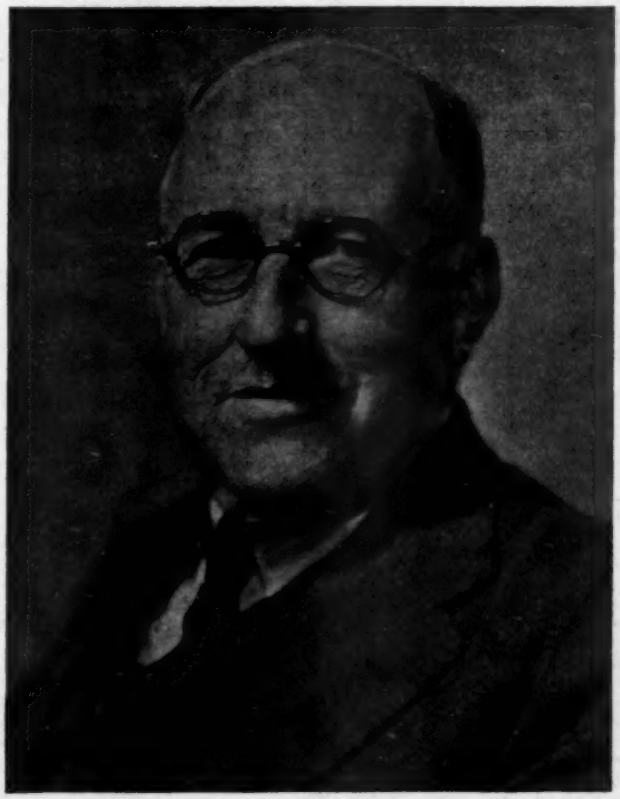
Whitehead, James Cockburn, M.B., B.S., 1933 (Univ. Melbourne), 186, Gipps Street, Abbotsford, N.9.

Obituary.

FREDERICK WILLIAM GREEN.

WE are indebted to Dr. H. Boyd Graham for the following account of the career of the late Dr. Frederick William Green.

It has come as a great shock to his many friends to hear of the death of "Freddie" Green, which occurred on November 8, 1937, from coronary thrombosis after a brief illness. Some of us knew that he had had symptoms of serious heart disease for some time, but he made light of his troubles and carried on his work to the end. Frederick William Green was born at Richmond, Victoria, in 1880. His father, the late Reverend Samuel Isaac Green, was the clergyman at the Lennox Street Congregational Church. Fred was an outstanding scholar at Camberwell Grammar School, being *dux* from 1895 to 1897. After one year at Wesley College he entered on the medical course at the University of Melbourne in 1899 and graduated M.B., B.S. in 1903. During the days at school and university he was well known as a good sportsman, particularly at cricket and tennis, at which sports he represented school and university in the senior teams.



After a year at the Melbourne Hospital as a resident medical officer, he went to Western Australia and assisted Dr. Trethowan at Perth for a few months. During this time he represented Western Australia at the interstate tennis competition. He returned to Victoria and practised in Charlton until, in 1913, he moved to Korumburra, where he continued to practise until he came to Malvern in 1920. Both at Charlton and at Korumburra his professional work was of a very high order and he was universally loved and respected. During the War he volunteered for active service repeatedly, but was rejected by the authorities on account of chronic middle ear trouble. He made amends for this disappointment by working hard, doing the work of two other men in Korumburra who had enlisted. This excessive work imposed a strain which probably undermined his health. He was a man of very high principles and refused to countenance anything remotely suggestive of expediency or subterfuge in any aspect of his professional work or of his duties as a citizen.

From the time he commenced to practise at Malvern he became actively associated with anæsthetic work as a specialty. From 1920, when he became an assistant anæsthetist at the Melbourne Hospital, and particularly from 1922, when he was appointed senior honorary anæsthetist at that hospital, his reputation for this class of work grew rapidly and extensively. He was an honorary anæsthetist at the Eye and Ear Hospital and at the Women's Hospital in addition, and published several valuable papers concerning anæsthesia. For many years he practised his specialty in Collins Street and came to be recognized as a leader throughout Australia. His services were sought by the Victorian surgeons for operations presenting the greatest difficulties. Many of his professional colleagues are indebted to him for his generosity and skill when they themselves or members of their families required anæsthesia. This duty to his colleagues he considered a privilege and an honour, but it imposed a great strain on his strength and energy. In 1935 he obtained the Diploma of Anæsthesia of London and in 1937 the Fellowship of the International College of Anæsthetists of America (F.I.C.A.).

Dr. Green came of a family brilliantly successful at many branches of sport, and as a young man was a first-class cricketer and tennis player. Later, he played a very good game of golf, billiards, bowls and bridge, in all of which he excelled without much effort. Like his brother "Tommy", whose death we deplored earlier this year, he was popular and was gifted physically and mentally. He realized that happiness was a twin; he won joy by sharing it. He was an ideal husband and father and was worshipped by his family and loved by his friends. He leaves a widow, a son, who is a solicitor in Tasmania, and two daughters, to whom we offer our deep sympathy.

Sir Alan Newton writes:

Dr. F. W. Green was aware for some years before his short fatal illness that he suffered from cardio-vascular disease similar to that which had already caused the deaths of some of his brothers and sisters. With quiet courage he decided to carry on with his work, preferring to die in harness rather than to prolong his days by an existence of semi-invalidism. Having made this decision, he never talked about his health, but carried on his incomparable work as an anæsthetist, infusing, as ever, a spirit of cheerful optimism in his patients and, in surgeons with whom he worked, a feeling of confidence that, whatever else might betide, anæsthetic difficulties would not be added to the problems which confronted them. It was my privilege to be closely associated with Dr. Green for a number of years. During this time he gave some thousands of anæsthetics for me in private practice and at the Royal Melbourne Hospital, and I cannot remember a single case in which trouble could justly be attributed to his work as anæsthetist, though I vividly recall more than one instance in which a calamity was averted by his prompt and skilful action. It has been my good fortune to work with several very good anæsthetists, but Dr. Green was generally accepted as *primus inter pares*. He was equally at home with every type of anæsthesia and fitted the anæsthetic to the needs of the patient. It has been stated

that ethylene and oxygen is an unsuitable anæsthetic for upper abdominal operations; Dr. Green gave this anæsthetic for me successfully on many occasions for such cases. I have often claimed that nitrous oxide and oxygen is the best form of anæsthetic for patients suffering from exophthalmic goitre; I must qualify this opinion by the statement that it is true only if the gas be given as he gave it. Shortly before his death he was exhibiting equal skill in the use of cyclopropane anæsthesia. Despite his proficiency in the use of new types of anæsthetics, he held fast to the belief that ether, properly administered, should remain the chief weapon of the anæsthetist, nor was he neglectful of the claims of chloroform in suitable cases. All this can be shortly summarized in the statement that "it is not the anæsthetic that matters: it is the anæsthetist". Dr. Green was undoubtedly the anæsthetist.

It was typical of his high sense of duty that he should have rejected the advice of his physician to lighten his load by relinquishing his charitable work at public hospitals. He continued his work at the Royal Melbourne Hospital until the end and earned the gratitude of all his colleagues by his untiring and successful efforts to improve the standard of teaching of students in anæsthesia. His work in this direction was by no means confined to the teaching of students, for I soon acquired the salutary knowledge that on my operating afternoons at the hospital the attention of visiting doctors was frequently directed more to the work of the quiet man behind the anæsthetist's screen than to my operative efforts.

During his life I tried on many occasions to tell him how much I valued his help. He would never listen to me. Now that he is dead I feel that lack of skill in the use of words has made me equally impotent adequately to express my gratitude. One week before his death, a woman, who had never seen him, asked, as did many others, that he should be specially engaged to give her the necessary anæsthetic. She entered hospital on the day he died and, when her family doctor and I saw her that night, she cried: "Dr. Green is dead. Whatever is to become of me?" I and the other surgeons with whom he worked can only echo that tribute to his deserved reputation.

Dr. R. W. Chambers writes:

The death of Fred Green means to the medical profession the loss of its most accomplished and experienced anæsthetist. There is no need for me to enlarge on his work. It was too well known to need this. It was with a great sense of security and confidence that one operated with Green giving the anæsthetic. No patient was too ill or the risk too great for him to refuse to give an anæsthetic if it was required. There are many people alive today because of his skill and judgement with the anæsthetic bottle. His work was of prime importance to him, and even during the last few years, when, I am sure, there were many occasions when he would have liked to have worked less hard and to have had more leisure time, yet his services were in such demand that, even though it probably shortened his life, he freely gave thereof. In spite of this very busy side of his life he found time to interest himself in art, literature and music. He was also a keen botanist, many of his happiest hours being spent in his "shack", as he called it, in the hills amongst his beloved bulbs and flowers. Some of the hours that I will always remember as being amongst the pleasant ones of my life were those spent on the golf links with him. During the latter years of his life, when his interest in competitive golf had waned (he was at one time on a very low mark) he was the prime mover in urging his more intimate friends to make breaks in the middle of the week for a game of golf. Without his influence there are many of us who would not have taken this time and enjoyed it and benefited thereby. He was one of the most charming of companions, always exercising a real influence for good, wherever he was. And so passes one of Nature's truly fine gentlemen, leaving behind him many sorrowing friends who will regret deeply the fact that never more will they enjoy his company.

To his wife and family go our very deepest sympathy in this very great loss that they have sustained.

Mr. W. Allan Hailes writes:

The untimely death of Dr. F. W. Green has left a gap in the medical profession in Melbourne which is realized personally by a large circle of friends, colleagues and former students; a gap which will be difficult indeed to fill. Within my knowledge of the medical profession of Victoria it has been given to few of its members to be as universally liked and esteemed as Dr. Green. Of a retiring disposition, this originated from his character and nature, which appealed to all. Human to a degree, Dr. Green was seldom, if ever, heard to say an unkind word of anyone, more especially of any member of the profession. Nevertheless he was a very shrewd observer and sound judge, both of men and methods, and his opinion, if sought with reason, was never withheld.

Transferring to Melbourne from Korumburra about seventeen years ago, Dr. Green practised anæsthesia as a specialty and quickly attained a leading position—indeed the leading position in that branch of medicine in this city. This position he maintained with a kindly dignity that endeared him to all, and with all the attributes of a leader in medicine. A recognized leader, jealousy never at any time entered his nature and not only did he give limitless time to the teaching of anæsthesia to students at the Royal Melbourne Hospital, but at all times his knowledge and help were available to others in the profession and to junior members of his own specialty. It has been truthfully said of him that it gave him as much pleasure to help a junior surgeon with a difficult case as it did to help a senior member of the profession. Under all conditions his kindly nature and disposition were always the same; whatever the emergency or embarrassing position, he could be trusted for the kindly action or word that kept the team working as a whole.

Dr. Green entered anæsthesia as a specialist at the period when gaseous anæsthetics, though established in other countries, were not in general use in Australia. In conjunction with some of his colleagues, his interest, example and efficiency were leading factors in popularizing those methods and establishing gaseous anæsthesia in Melbourne at its present high state of efficiency.

The time he spent in instructing students in the clinical school of the Royal Melbourne Hospital was limitless, and he availed himself of every opportunity of so doing. A long line of former students will regret the passing of one who was not only their teacher, but an inspiration and an example to anyone on the threshold of a professional career.

Dr. Green, being a member of a family that excelled at sport, was a keen cricketer, footballer, bowler and golfer of no mean ability. He was an outstanding bridge player and a gardener. These associations gave him a diversity of interests that appealed to all and ensured him a ready entry to any company.

To his widow and family all will extend their sympathy.

ANDREW DAVIDSON.

We regret to announce the death of Dr. Andrew Davidson, which occurred on February 7, 1938, at Sydney, New South Wales.

Correspondence.

THE COSMETIC VALUE OF THE UMBILICUS.

SIR: During the recent discussion of the medical congress on the treatment of umbilical hernia, I stressed a medico-legal consideration, which I thought seldom entered the

surgeon's mind when operating for the relief of such herniæ. The letter enclosed was read as evidence that a definite cosmetic value was sometimes set on the navel, either by the patient herself or her husband, so that, before undertaking treatment the patient should be warned of the possibility of finding only a linear scar where a dimple used to appear.

I was surprised to learn that many other surgeons had been made aware of their patients' post-operative dissatisfaction. The letter itself is one of those gems of composition that we all treasure up, and as so many of my colleagues have asked me for a copy, I give this as another reason for asking you to publish it.

Dear Sir,

On the 23 of Jan I brought my wife in to the Hospital to be attended for a strangulated herneia on the 25 of Jan Dr Close performed an operation without firstly consulting me or otherwise obtaining my wifes consent not only operationg for herneia but also cutting away the whole nable without any one's consent making her appearance look as if the chinese vandals had had hold of her, as I had her examined by several doctors before and after same I expect compensation for this deed otherwise I am going to start proceedings in court to recover damages as I cannot bear to have her near me as she is I will have to send her somewhere else as it makes me ill to look at her as she is. Needless to say I was not told about this after the operation nor was my wife the first I knew about this affair was when she came home and asked me to tighten the binder for her and asked me to look if the doctors had not cut her nable right out. I have never heard of such an act of gross insolence it is only equal to Hitler's sterilisation act. I will wait 6 days for an answer to this letter before putting it in the hands of a solicitor.

Yours truly,

.....

P.S.

The operation cut looks as if it had been chewed by a dog.

Although, after removal of such a huge mass of abdominal excrescence which one so often must do, the old proverb must be quite applicable, still it is poor consolation to be told: "Half a wife is better than no wife at all."

Yours, etc.,

W. JOHN CLOSE.

Adelaide,
January 27, 1938.

Post-Graduate Work.

QUEENSLAND POST-GRADUATE COURSE.

THE Queensland Post-Graduate Committee advises that the annual refresher course will be held in Brisbane from Friday, May 27, to Friday, June 3, 1938. Details of the programme will be made available later.

Congresses.

THE THIRD INTERNATIONAL CONGRESS FOR MICROBIOLOGY.

THE third International Congress for Microbiology will be held at the Waldorf-Astoria Hotel, New York City, on September 2 to 9, 1939, under the auspices of the International Association of Microbiologists.

Dr. T. M. Rivers, of the Rockefeller Institute for Medical Research, New York City, is President. Dr. M. H. Dawson, College of Physicians and Surgeons, 620, West 168th Street, New York City, is General Secretary. Dr. Kenneth Goodner, of the Rockefeller Institute for Medical Research, New York City, is General Treasurer.

The congress will be composed of the following nine sections:

1. General biology: variation and taxonomy. Convener, C.-E. A. Winslow.
2. General biology: microbiological chemistry and physiology. Convener, Stuart Mudd.
3. Viruses and viral diseases. Convener, W. A. Sawyer.
4. Rickettsiæ and rickettsial diseases. Convener, Hans Zinsser.
5. Protozoology and parasitology. Convener, H. W. Stunkard.
6. Fungi and fungous diseases. Convener, B. O. Dodge.
7. Medical and veterinary bacteriology. Convener, F. P. Gay.
8. Agricultural and industrial microbiology. Convener, S. A. Waksman.
9. Immunology. Convener, M. Heidelberger.

The registration fee will be five dollars, which will not include the cost of a banquet ticket or a copy of the proceedings of the congress.

A world's fair will be held in New York City during the summer of 1939. Consequently those who wish to attend the Congress for Microbiology should make plans promptly. The American Express Company, the official travel agency for the congress, will be glad to assist in such plans.

Proceedings of the Australian Medical Boards.

TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

Hughes, Arthur Russell, M.B., B.S., 1937 (Univ. Melbourne), General Hospital, Launceston.
Jenkins, Percy Northumberland, M.B., B.S., 1937 (Univ. Melbourne), General Hospital, Launceston.
Whitaker, Henry, M.B., B.S., 1928 (Univ. Melbourne), Devon Hospital, Latrobe.

THE GIBSON FUND, QUEENSLAND.

THE Council of the Queensland Branch of the British Medical Association has instituted a fund to assist in the education of the children of the late Dr. Leslie Wylie Norman Gibson, whose death was recently recorded in these pages.

Although he had not been for long in Queensland, Dr. Gibson faithfully served the Branch in the capacity of honorary secretary for a considerable period before his death.

Donations to the fund may be sent to the Honorary Secretary of the Queensland Branch of the British Medical Association, British Medical Association House, 225, Wickham Terrace, Brisbane, B.17.

A SPEECH THERAPY COURSE IN NEW SOUTH WALES.

THE Hospitals Commission of New South Wales has decided to establish a speech therapy training course. In speech therapy is included the treatment of speech defects which comprise such conditions as stammering, lisping, retarded or infantile speech, cleft palate speech, aphasia, speech disorders due to psychological causes.

At present any person desiring to train in speech therapy has to go abroad for the necessary study.

If sufficient students are forthcoming it is intended to commence this course in March, 1938. The course will include the following subjects: phonology, diction, neurology and psychology of normal speech, phonetics, the treatment of all speech defects, psychology, the treatment of cleft palate speech and other allied conditions. The practical work will be carried out at the speech clinic of the Royal Alexandra Hospital for Children, Sydney.

Any information regarding this course can be obtained from the Secretary of the Hospitals Commission of New South Wales, Agriculture Building, Farrer Place, Sydney, New South Wales.

Diary for the Month.

FEB. 15.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 22.—New South Wales Branch, B.M.A.: Medical Politics Committee.
FEB. 23.—Victorian Branch, B.M.A.: Council.
FEB. 24.—South Australian Branch, B.M.A.: Branch.
FEB. 25.—Queensland Branch, B.M.A.: Council.
MAR. 1.—New South Wales Branch, B.M.A.: Organization and Science Committee.
MAR. 2.—Western Australian Branch, B.M.A.: Council.
MAR. 2.—Victorian Branch, B.M.A.: Branch.
MAR. 3.—South Australian Branch, B.M.A.: Council.
MAR. 4.—Queensland Branch, B.M.A.: Branch.
MAR. 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
MAR. 11.—Queensland Branch, B.M.A.: Council.
MAR. 15.—New South Wales Branch, B.M.A.: Ethics Committee and Medical Politics Committee.
MAR. 16.—Western Australian Branch, B.M.A.: Branch.
MAR. 22.—New South Wales Branch, B.M.A.: Council (Quarterly).
MAR. 23.—Victorian Branch, B.M.A.: Council.
MAR. 24.—South Australian Branch, B.M.A.: Branch.
MAR. 24.—New South Wales Branch, B.M.A.: Annual Meeting.
MAR. 25.—Queensland Branch, B.M.A.: Council.
MAR. 29.—New South Wales Branch, B.M.A.: Council (Election of Officers and Standing Committees).

Medical Appointments.

Dr. J. Bell has been appointed Government Medical Officer at Aramac, Queensland.

* * *

Dr. B. F. R. Stafford has been appointed Medical Superintendent, Hospital for the Insane, Goodna, Queensland.

* * *

Dr. W. P. H. Parker has been appointed, under the provisions of *The Insanity Acts*, 1884 *to* 1935, and *The Public Service Acts*, 1922 *to* 1924, of Queensland, Medical Superintendent, Hospital for the Insane, Ipswich.

* * *

Dr. C. T. C. de Crespigny has been appointed Honorary Consulting Physician at the Adelaide Hospital, Adelaide, South Australia.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants. *locum tenentes* sought, etc., see "Advertiser," pages XX to XXII.

ALFRED HOSPITAL, MELBOURNE, VICTORIA: Medical Officers.
DEPARTMENT OF INSPECTOR-GENERAL OF HOSPITALS, ADELAIDE, SOUTH AUSTRALIA: Resident Medical Officer.
ROYAL HOSPITAL FOR WOMEN, PADDINGTON, NEW SOUTH WALES: Resident Medical Officer.
TAMWORTH BASE HOSPITAL, TAMWORTH, NEW SOUTH WALES: Resident Medical Officer.
THE BENEVOLENT SOCIETY OF NEW SOUTH WALES, SYDNEY: Honorary Officers.
TOOWOOMBA HOSPITALS BOARD, TOOWOOMBA, QUEENSLAND: Resident Medical Officer.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135 Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178 North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

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